# CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS

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*Dedicated*

*to*

*my Family*

*&*

*Teachers*

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**“As we express our gratitude, we must never forget that the highest appreciation is not to utter words, but to live by them.”**

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**Dr. Rashi Aggrwal**

# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| AFB | - | Acid Fast Bacilli |
| CA 125 | - | Cancer antigen 125 |
| CA 19-9 | - | Carbohydrate antigen 19-9 |
| CEA | - | Carcinoembryonic antigen |
| CI | - | Confidence interval |
| CT | - | Computed Tomography |
| DAB | - | Diaminobenzidine |
| DPX | - | Distyrenedibutyl phthalate xylene |
| EUS | - | Endoscopic ultrasound |
| FNA | - | Fine Needle Aspiration |
| FNAC | - | Fine Needle Aspiration Cytology |
| H & E | - | Hematoxylin& eosin |
| IHC | - | Immunohistochemistry |
| MGG | - | May Greenwald Giemsa |
| MRI | - | Magnetic Resonance Imaging |
| PAP | - | Papanicolau Stain |
| PAS | - | Periodic Acid Schiff Stain |
| PBS | - | Phosphate buffered saline |
| SPSS | - | Statistical Package for the Social Science |
| USG | - | Ultra Sonography |
| ZN | - | Ziehl–Neelsen |

# ABSTRACT

**Introduction**: Mediastinal lesions are uncommon in routine clinical practice. They can be broadly classified into non- neoplastic and neoplastic lesions. FNAC has been increasingly utilised as a minimally invasive procedure for the diagnosis of mediastinal lesions.

**Aims & Objectives**: To study the cytomorphological features of all mediastinal lesions and to correlate them with the clinico-radiological profile, histopathological findings and IHC wherever possible.

**Material & Methods**: This study was conducted in Dayanand Medical College And Hospital, Ludhiana for a period of 5 years from 1$^{st}$July 2016 to 30$^{th}$June 2021 (Three and a half years retrospective from 1st July 2016 to 31$^{st}$ December 2019 and one and half years prospective from 1$^{st}$ January 2020 to 30$^{th}$ June 2021) .The smears received in the cytology laboratory from image guided FNAC of mediastinal lesions were analysed and cell blocks were made wherever possible. Relevant special stains were used. During this period all specimens were correlated with clinical and radiological findings & histopathology and IHC was used wherever possible.

**Results**: A total of 102 cases of mediastinal lesions were analysed with slight male predominance (M:F ratio -1.4:1). Fever and cough (43.14%) were the most common clinical presentations. Cytological smears were categorized as Non -diagnostic (27.45%), Non –neoplastic (34.31%) and neoplastic (38.24%). Non- neoplastic category comprised of 35 cases in which definitive diagnosis comprised of Granulomatous inflammation (77.14%), Reactive hyperplasia of lymph node (8.57%), Benign cyst (5.71%), Acute suppurative pathology (5.71%) and Non-specific inflammation (2.85%). In the malignant category which constituted 39 cases of the total, maximum cases were of lymphoma (28.20%) followed by metastatic tumor (23.07%), carcinoma NOS (17.94%), thymoma(10.25%), malignant round cell tumor(10.25%) and germ cell tumors (5.12%). Cyto-histopathological correlation was done in 35.29% of cases and and limited concordance within the neoplastic category was seen in 11.54% of cases.

**Conclusion**: FNAC for mediastinal lesions has become an established diagnostic procedure with excellent results worldwide. The main aim is to categorise the lesion as neoplastic or non neoplastic. This will enable the clinicians to manage and treat the cases effectively .In this study we also plan to correlate the cytomorphological features with the clinico-radiological findings, histopathological findings and IHC wherever possible.



**Keywords**: Mediastinal Lesions, FNAC, Clinico-Radiological, Histopathological findings

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# INTRODUCTION

The mediastinum is the central part of thoracic cavity which is bounded by pleural sacs, sternum, and vertebral bodies.[1] The mediastinum extends antero-posteriorly from the sternum to the spine and from the thoracic inlet down to the diaphragm. It contains various structures such as heart, thymus, lymph nodes, major blood vessels, nerves, trachea, and esophagus. It has been divided into four compartments, i.e. superior, anterior, middle and posterior. Mediastinal lesions present with vague chest complaints and or signs and symptoms due to compression and invasion of mediastinal structures. Various benign and malignant diseases manifest as mediastinal mass and pose diagnostic challenge. Mediastinum is a complex anatomic area playing host to a wide variety of neoplastic and non- neoplastic lesions with different management plan to facilitate timely treatment. Adequate knowledge of the mediastinal compartments and precise localization and characterization of the lesions with the help of radiological modalities like CT scan/MRI thorax may help narrow the differential diagnosis. FNAC and/or core needle biopsy are minimally invasive, safe, easy to perform techniques that allow adequate tissue sampling with high diagnostic accuracy and least risk to the patients. Usual symptoms at presentation are cough, chest pain, fever with chills and dyspnea. Localising symptoms are secondary to tumour invasion (respiratory compromise, paralysis of the limbs, diaphragm and vocal cords, Horner syndrome, superior vena cava syndrome), while systemic symptoms are typically due to the release of excess hormones, antibodies or cytokines.

The initial evaluation of a suspected mediastinal mass consists of a thorough history and physical examination, supplemented by laboratory and imaging studies. The clinical approach includes in-depth history of symptoms, demographic features, and close search for physical signs. The currently available modalities for further evaluation include chest radiographs, ultrasound, CT scan, magnetic resonance imaging (MRI),

and nuclear medicine studies. Chest X-ray with posteroanterior and lateral views is indicated in all cases. It provides information on the size, anatomical location, density, and at time composition of the mass. CT scan with intravenous contrast enhancement is an essential tool to evaluate further that provides additional information, i.e., relationship of the mass with adjacent structures, vascularity within the mass, content, and nature (cystic or solid) of the mass. MRI provides useful information in evaluating spinal, vascular, or cardiac invasion. An excellent soft tissue contrast also designates magnetic resonance imaging (MRI) as an ideal tool to evaluate tumours of the mediastinum[2] It is more sensitive than CT for evaluating the involvement of the neural foramen or spinal canal invasion in posterior mediastinum and for evaluating thyroid masses. Given its superior tissue contrast resolution and lack of ionizing radiation, MRI has been increasingly utilized for mediastinal mass evaluation nowadays.[3] Transesophageal echocardiogram, barium swallow, and testicular ultrasound may be needed in selected cases. Nuclear medicine studies available for mediastinal mass evaluation primarily include positron emission tomography (PET) often co registered with CT (PET/CT) and metaiodobenzylguanidine imaging. A combination of these often helps to narrow the possibilities when a mediastinal mass is detected on imaging. Laboratory studies or blood tumor markers can also help support a specific diagnosis.

Morphological assessment by fine needle aspiration cytology (FNAC) or histopathological examination is imperative prior to therapeutic intervention. The mediastinum is surrounded by many vital structures such as heart and great vessels. Therefore many precautions are needed to perform FNAC of the mediastinal lesions. In fact, a team of experts consisting of radiologists, cytologists, physicians and surgeons is required to perform mediastinal FNAC. Usually ultrasonologically guided, CT or fluoroscopic guided FNAC are performed. Aspirated material can be collected for cell block, flow cytometry, electron microscopy and microbial culture. Sections from the cell block could be

used for immunohistochemistry and this is one of the corner stones in ancillary technique. Material collected for flow cytometry could be processed after the initial diagnosis of lymphoma is rendered on FNAC smears. This stepwise logistic approach is very helpful in major diagnostic categorization of mediastinal tumors.

Mediastinal masses are rare and can present as a challenge for clinicians. Clinicians need to be vigilant as a lot of times diagnosis can be delayed and patients can land up with features of respiratory distress due to compression of trachea or carina. Anterior mediastinal masses are most common site followed by posterior mediastinum which mostly comprises of neurogenic tumors. Middle mediastinal masses are very rare and are generally benign cysts. Surgical resection of the mass is required in most of the cases

Although FNAC is a cost effective tool for the establishment of pre-operative diagnosis of mediastinal masses, there is a complexity and technical difficulty associated with this technique owing to the narrow anatomic space of mediastinum. Despite being a well-delineated narrow space, the diversity of lesions arising in the mediastinum pose an interesting diagnostic challenge for the clinicians, radiologists and pathologists.

# AIMS & OBJECTIVES

1. To study the detailed cytomorphological features of all mediastinal lesions.
2. To correlate them with clinico-radiological profile and histopathology with IHC wherever possible.

# REVIEW OF LITERATURE

## ANATOMICAL PERSPECTIVES:

The mediastinum is the median portion of the thoracic cavity, occupying the space between the lungs and containing all of the thoracic structures such as the heart and major vessels, esophagus, trachea and main bronchus, thymus, venous, lymphatic structures and nervous tissue except the lungs. It is limited by the pleura of the right and left lungs laterally, by the sternum anteriorly and by the vertebrae and ribs posteriorly. This space is divided into the superior and inferior mediastinum by an imaginary horizontal plane, passing anteriorly from the sternal angle, and posteriorly from the lower border of T4 vertebra. The inferior mediastinum is further divided into anterior, middle and posterior parts by anterior and posterior fibrous pericardium [4]Superior mediastinum bordered by the thoracic inlet superiorly, transverse thoracic plane (the plane of Ludwig) or sternal angle inferiorly, medial border of the pleural sacs laterally, dorsal surface of the sternum anteriorly, and ventral surface of the first four thoracic vertebral bodies posteriorly. Anterior mediastinum bordered by the pericardium posteriorly, medial border of the pleural sacs laterally, and the sternum, transversus thoracis muscles, and fifth, sixth, and seventh left costal cartilages anteriorly. Middle mediastinum formed by the borders of the pericardial sac anteriorly and posteriorly, reflected to the medial borders of the pleural sacs bilaterally, transverse thoracic plane superiorly, and thoracic surface of the diaphragm inferiorly .Posterior mediastinum bordered by the pericardium anteriorly, the thoracic surface of the diaphragm inferiorly, the transverse thoracic plane superiorly, the bodies of the fifth to the twelfth thoracic vertebrae posteriorly, and the pleural sacs laterally.

Many mediastinal lesions are asymptomatic and discovered as an incidental finding on chest X ray. Despite its limited extent, the mediastinum is the site of a variety of inflammatory and neoplastic processes. Topography is an important factor in making a diagnosis

because the different compartments of the mediastinum harbour different tumors or lesions. Age of the patient is also of great importance due to age-related prevalence of certain lesions. Aspiration cytology helps to determine whether the space occupying lesion is neoplastic, inflammatory or a malformation. Cytological findings must be complemented with clinical history, laboratory investigations and radiological findings. Additional investigations such as immunocytochemistry, flow cytometric immunophenotyping, and tumor markers help in confirmation of diagnosis. Stepwise algorithmic approach provides more definitive diagnosis in majority of the cases.

Each region of the thoracic mediastinum contains unique structures. Listed below are the different structures of the thoracic mediastinum:

- Superior Mediastinum:
    - Organs: thymus, trachea, esophagus
    - Arteries: aortic arch, brachiocephalic trunk, left common carotid artery, left subclavian artery
    - Veins and lymphatics: superior vena cava, brachiocephalic veins, the arch of the azygos, thoracic duct
    - Nerves: left and right vagus, recurrent laryngeal, cardiac, left and right phrenic nerves
- Anterior Mediastinum:
    - Organs: thymus
    - Arteries: Branches of internal thoracic vessels
    - Veins and lymphatics: branches of internal thoracic vessels, parasternal lymph nodes
- Middle Mediastinum:
    - Organs: the heart and its great vessel roots, trachea and main bronchi
    - Arteries: ascending aorta, pulmonary trunk, pericardiacophrenic arteries
    - Veins and lymphatics: superior vena cava, pulmonary veins, pericardiacophrenic veins

    - Nerves: phrenic nerve, vagusnerve ,sympathetic chain
- Posterior Mediastinum:
    - Organs: esophagus
    - Arteries: descending thoracic aorta
    - Veins and lymphatics: azygos hemiazygos veins, thoracic duct
    - Nerves: vagus nerve, splanchnic nerve, sympathetic chain

Mediastinal mass lesions include a wide diversity of tumours which posea diagnostic and therapeutic challenge to pulmonologists and thoracic surgeons and account for 3% of the tumours within thechest.[5] The tissue of origin can be thymic, hematopoietic, lymphatic, germinal, neurogenic or mesenchymal. Secondary or metastatic tumors in the mediastinum generally occur more frequently than primary tumors.[6,7]

**PRESENTATION**

Mediastinal mass can be asymptomatic or produce a wide range of non-specific symptoms. Patients with mediastinal masses either present with local or systemic symptoms due to the compression or invasion.[8] Such symptoms include cough, dyspnea, dysphagia and hoarseness of the voice as a result of compression of adjacent structures. They can also present as surgical emergencies like superior vena caval obstruction and stridor. In such cases, the superior vena cava is compressed, leading to Superior Vena Cava Syndrome and a patient will present with dyspnea, cough, distended neck veins and facial swelling. These symptoms are collectively referred to as symptoms of mediastinal obstruction. As the mediastinal space is narrow, any mass originating here will compress the surrounding structures. Thus a growing mass in the mediastinum can be life-threatening.

## INVESTIGATIONS

Diagnosis of mediastinal tumors require an integrated clinical, radiological, cytological and histological approach. The clinical approach includes in-depth history of symptoms, demographic features, and close search for physical signs.

### Radiological Investigations

The currently available modalities for further evaluation include chest radiographs, ultrasound, CT scan, magnetic resonance imaging (MRI), and nuclear medicine studies. Chest X-ray with posteroanterior and lateral views is indicated in all cases. It provides information on the size, anatomical location, density, and at time composition of the mass.

CT scan with intravenous contrast enhancement is essential to provide additional information, i.e., relationship of the mass with adjacent structures, vascularity within the mass, content, and nature (cystic or solid) of the mass. Characterisation on CT is based on specific attenuation of air, fat, water and calcium.

MRI provides useful information in evaluating spinal, vascular, or cardiac invasion. It is more sensitive than CT for evaluating the involvement of the neural foramen or spinal canal invasion in posterior mediastinum and for evaluating thyroid masses. Given its superior tissue contrast resolution and lack of ionizing radiation, MRI has been increasingly utilized for mediastinal mass evaluation nowadays.[9] Diffusion-weighted MRI (DWI) is another special application that unveils minute metabolic and biophysical differences between tissues

Transesophageal echocardiogram, barium swallow, and testicular ultrasound may be needed in selected cases. Nuclear medicine studies available for mediastinal mass evaluation primarily include positron emission tomography (PET) often coregistered with CT (PET/CT) and metaiodobenzylguanidine imaging.

Nuclear scans and biochemical studies are useful in diagnosing and evaluating the suspected thyroid lesions, catecholamine-secreting

tumor, and malignancy. Lab investigations: Complete hemogram in addition to the following tumor markers are recommended when thymoma is considered. Also recommended are serum levels of β HCG, AFP (to rule out Germ cell tumors), T3, T4, TSH, gamma globulins, ACTH, ADH (to rule out Neuroendocrine tumor). One must obtain serum anti-acetylcholine receptor antibody to assess for Myasthenia Gravis.

**Pathological investigations**

Clinical assessment along with radiographic imaging often narrows the differential diagnosis, but definitive tissue diagnosis is often required before initiating therapy. There are several modalities to obtain tissue samples for cytological or histological diagnosis of mediastinal lesions.

These include percutaneous image-guided transthoracic needle aspiration and/ or biopsy (under CT or ultrasound guidance); endoscopic biopsy without ultrasonography (transbronchial through a fiberoptic bronchoscope); endoscopic aspirate and/or biopsy with ultrasonography, i.e., bronchoscopically (EBUS) or through the esophagus (endoscopic ultrasound [EUS]) using a fine needle.

The percutaneous transthoracic FNAC and/or biopsy of the mediastinal lesion under local anesthesia are minimally invasive, cost-effective, easy to perform, well tolerated and associated with low complication rates when performed under ultrasound or CT scan guidance. The accuracy of transthoracic biopsy in the diagnosis of mediastinal lesions ranges from 75% to 90%.[10]

These procedures allow adequate tissue sampling with the least risk to the patients and have added benefit of reduced medical care cost as they substitute the need for more extensive diagnostic surgical procedures and reduce the hospital stay.

Clinical background and radiological correlation further support the cytopathologist to reach diagnosis. Although other diagnostic modalities such as transsternal approach, transbronchial approach,

EUS of the esophagus, and EBUS approaches are recently introduced,[11] but the conventional transthoracic FNA and/or biopsy for mediastinal lesion still hold its role due to easy procedure, low cost, easy to train, and learn in low infrastructure units.

Precise location and site for FNAC or core biopsy are of utmost importance in view of complex structures in the mediastinum. Thus imaging techniques are often required to guide the biopsy needle to sample the target area.[12] Clinical history, physical examination, radiological findings, and location of masses in the mediastinum help in making the tentative diagnosis, but tissue diagnosis is the gold standard for the final diagnosis and for planning the management of mediastinal lesions.[13]

An accurate and early tissue diagnosis is warranted in mediastinal lesions to separate malignant lesions from the nonneoplastic and benign conditions as the treatment goals are different. These lesions often pose diagnostic problems because of their location and difficult access.

Most common lesions in different anatomical compartments of the mediastinum are enumerated below:[14]

**Superior Mediastinum:**

- Thymoma
- Thymic cyst
- Malignant lymphoma,
- Thyroid lesions
- Parathyroid adenoma

**Anterior Mediastinum:**

- Thymoma
- Thymic cyst
- Germ cell tumour
- Lymphoma
- Paraganglioma

- Hemangioma
- Lipoma.

**Middle Mediastinum:**

- Pericardial cysts
- Bronchogeniccysts
- Malignant lymphoma

**Posterior Mediastinum:**

- Neurogenic tumours
    i. Schwannoma
    ii. Neurofibroma
    iii. Ganglioneuroma
    iv. Ganglioneuroblastoma
    v. Neuroblastoma
    vi. Paraganglioma
- Gastroenteric cyst.

The incidence of mediastinal tumors is 43-54% in the anterior mediastinum, 11.4-31.8% in the middle mediastinum and 8.57-26% in the posterior mediastinum.

**Lesions in anterior mediastinum**

Thymus is a lobulated organ and covered by capsule and it is divided into cortical and medullary portions. Two major cell types are endodermally derived epithelial cells and bone marrow derived lymphocytes. Structures known as Hassall's corpuscles, which are similar to squamous pearls and are dispersed throughout the thymus are formed by epithelial cells .The thymus acts as a primary lymphoid organ and a site for T-cell maturation. The thymus undergoes progressive involution as a person grows older, which precludes the high incidence of thymomas in older patients.[15]

**Thymoma**

Thymomas are the most common tumors arising from the anterior mediastinum.[16] Thymomas have no gender predilection and can occur at any age. A thymoma is a slow growing thymic epithelial tumor in which the epithelial component exhibits no overt atypia and retains histologic features specific to the normal thymus. Most tumors contain a proportion of epithelial cells and lymphocytes, although the majority of thymomas are completely encapsulated.

Approximately half of the thymomas discovered are asymptomatic, whereas the other half present with paraneoplastic syndrome[17] such as Myasthenia Gravis, Polymyositis, Systemic Lupus Erythmatosis, Rheumatoid Arthritis, Thyroiditis, Sjogren's syndrome, pancytpenia, Syndrome of inappropriate antidiuretic hormone secretion, Pure Red Cell Aplasia, and Hypogammaglobinemia.

25% to 40% of patients with thymoma present with myasthenia gravis[18], and more than 15% of patients diagnosed with thymoma present with a paraneoplastic syndrome other than myasthenia gravis.[19]

Myasthenia gravis (MG), is the most common paraneoplastic syndrome. MG is an autoimmune neuromuscular disease caused by circulating autoantibodies that block acetylcholine receptors at the postsynaptic membrane.

There are several clinical and pathologic classification systems for thymomas but WHO is most commonly followed.

WHO Classification of Thymomas (2015)[20]

i. Type A thymoma including atypical variant
ii. Type AB thymoma
iii. Type B1 thymoma
iv. Type B2 thymoma
v. Type B3 thymoma
vi. Micronodular thymoma with lymphoid stroma

vii. Metaplastic thymoma
viii. Other rare thymomas

**(i)Type A Thymoma (Spindle Cell; Medullary)**

It is a thymic epithelial neoplasm composed of usually bland spindle/oval tumor cells with few or no admixed immature lymphocytes. Cytological smears contain only epithelial cells and can mimic other spindle cell lesions such as carcinoid tumor, low grade sarcoma, mesothelioma and stromal cells in lymphoma.

The appearance of this tumor can simulate that of a mesenchymal neoplasm, but the immunohistochemical and ultrastructural features are clearly those of an epithelial tissue. A peculiar feature of the neoplastic epithelial cells in type A thymomas is expression of CD20 in about half of them.[21]

**(ii)Type AB Thymoma (Mixed)**

It is a thymic epithelial neoplasm composed of a lymphocyte poor spindle cell (type A) component and a lymphocyte-rich (type-B-like) component with a significant population of immature T-cells. The relative proportion of the two components is highly variable. Patient age ranges from 11 to 89 years with a slight female predominance.

On histology type AB thymoma is usually well demarcated and is composed of highly variable mixture of lymphocyte poor type and a more lymphocyte rich type-B like component. These components either form discrete, separate nodules or are intricately intermingled.

On cytology, smears show a dual population of epithelial and lymphoid cells in variable proportion. A highly variable number of lymphocytes is intermingled with epithelial cells. The epithelial cells are polygonal, oval or spindly with moderate to abundant pale cytoplasm and bland vesicular nuclei.

**(iii)Type B1 Thymoma (Lymphocyte-Rich; Lymphocytic; Predominantly Cortical; Organoid)**

It resembles the normal functional thymus in that it combines large expanses having an appearance practically indistinguishable from normal thymic cortex in which cytologically bland thymic epithelial cells are evenly dispersed within a background of immature T cells and accompanied by areas resembling thymic medulla.[22]

On cytology, lymphocyte rich smears lead to the misdiagnosis of reactive lymph node, thymic hyperplasia or T lymphoblastic lymphoma. The presence of inconspicuous epithelial cells can suggest the diagnosis. The lymphocyte rich thymoma (B1 subtype) could be misdiagnosed as lymphoma.[23]

On IHC, the epithelial cells are diffusely positive for CK19, focally positive for CK7, CK8, CK14 and CK18 and negative for CK20. Almost all cases express p63 and PAX8. Lymphocytes are mostly immature T-cells and express normal cortical marker profile ie CD1a+, CD3+, CD4+, CD8+ and CD34-.

**(iv)Type B2 Thymoma (Cortical)**

It is a lymphocyte rich tumor composed of polygonal neoplastic epithelial cells set in a background of numerous immature T-cells. In this the neoplastic epithelial component appears as scattered plump cell, often including small (≥3 contiguous epithelial cells) clusters, with vesicular nuclei and distinct nucleoli among a heavy population of immature T cells.[24]

Like B1 thymoma, type B2 thymoma is lymphocyte rich resulting in a mixed lymphocyte–epithelial pattern.

On cytology, smears typically show isolated or clustered epithelial cells intermingled with numerous lymphocytes. Type B2 thymoma may be mistaken for reactive lymph node, thymic hyperplasia or T lymphoblastic lymphoma if epithelial cells are sparse due to poor sampling.

**(v)Type B3 Thymoma (Epithelial; Atypical; Squamoid; Well-Differentiated Thymic Carcinoma)**

This thymoma,is predominantly composed of mildly atypical epithelialcells having a round or polygonal shape admixed with a minor componentof immature T cells, resulting in a sheetlike growth of the neoplasticepithelial cells.[25] On histology, there is predominance of polygonal epithelial cells that form solid sheets having eosinophilic or clear cytoplasm and moderately atypical round to elongated sometimes grooved nuclei.

On cytology, smears show sheets of tumor cells with some size variation, round nuclei, inconspicuous nucleoli and rare admixed lymphocytes.

On IHC tumor cells express CK19, CK5/6, CK7, CK8 and CK10 but not CK20. CD57, p63, PAX8 are sometimes positive.

**(vi) Micronodular Thymoma with lymphoid stroma**

It is a thymic epithelial tumor characterised by multiple small tumor islands composed of bland spindle or oval cells that are surrounded by an epithelial cell-free lymphoid stroma which may contain lymphoid follicles. The lymphocytes are composed mainly of B cells and mature T cells, and the epithelial cells are generally negative for CD20, two findings that may be helpful in distinguishing micronodular thymoma from type AB thymoma.

**(vii) Metaplastic thymoma**is a rare subtype, it is a biphasic tumor in which solid areas of epithelial cells are variably well demarcated from cytologically bland, fibroblast-like spindle cells. There is absence or paucity of lymphocytes throughout the tumor. Rarely areas of sarcomatoid differentiation can be seen and is associated with high grade transformation.

**Thymic Carcinoma**

Thymic carcinoma is rare, constituting approximately 0.06% of thymic neoplasms.[26] Thymic carcinomas have a poor prognosis because they are usually discovered at an advanced stage.

They are aggressive epithelial tumors associated with a high incidence of local invasion and distant metastases (lung, liver, brain, and bone). Symptoms are more common than in thymomas, and patients frequently present with cough, chest pain, and shortness of breath.

The cytologic features, include cells having irregular configuration with abundant opaque eosinophilic cytoplasm and large nuclei with coarsely clumped chromatin, visible or even prominent nucleoli and sometimes mitoses. Necrosis is common.

They are very uncommon on cytology. It has a wide variety of morphological appearances including keratinizing and non keratinizing squamous cell carcinoma, sarcomatoid, anaplastic carcinoma, basaloid, mucoepidermoid, small cell carcinoma.

**Various other lesions of thymus are described as follows:**

**a)Thymic hyperplasia** - can be divided into two distinct histological types. True thymic hyperplasia is defined as enlargement of the thymus, which generally retains its normal shape. This disease entity is observed when a patient is recovering from some recent stress (such as chemotherapy, corticosteroid therapy, irradiation or thermal burns). The phenomenon, known as rebound hyperplasia, is defined as a greater than 50% increase in thymic volume over baseline after such stress.[27] Among patients who undergo chemotherapy, approximately 10–25% may develop rebound hyperplasia.

Needle aspirates of hyperplastic thymus yields a mixed population of lymphocytes that is unlikely to contain more than a few benign epithelial or spindle cells. And the cytological smears resemble those of reactive lymph nodes.

**b) Thymolipoma-** Thymolipomas are benign, slow-growing tumors that occur in the anterior mediastinum. Less than 10% of thymic lesions are thymolipomas. They are characterized by the presence of abundant adipose tissue in addition to thymic tissue. Surgical resection of a thymolipoma is curative with almost no chance of recurrence.[28]

**(c) Thymic cyst -** Thymic cysts represents 1% of all mediastinal masses.[29] Congenital cysts are derived from remnants of the thymopharyngeal duct, they may be unilocular or multilocular and may contain clear or straw colored fluid, or sometimes old blood. In contrast, acquired thymic cysts are much more common, tend to be multilocular and may arise in association with neoplasms such as thymomas, lymphomas or germ cell tumours. The cysts are thin walled and lined by epithelium that vary from flattened to cuboidal to columnar with or without cilia or by stratified squamous epithelium. The nature of the aspirate depends on the nature of the cyst contents and type of lining epithelium involved but it usually contains foamy histiocytes.

**GERM CELL TUMORS**

Germ cell tumours (GCTs*)* mainly arise in gonads and in the midline of the body as well, the mediastinum being the most common extragonadal site. Extragonadal GCTs (EGCTs) arise outside the gonads, typically midline in location and constitutes for only 2% to 5% of all GCTs.[30]

Germ cell tumors (GCTs) contain primitive germ cells that fail to migrate entirely during embryonic development.

WHO Classification of germ cell tumors of mediastinum (2015) [31]

a. Seminoma
b. Embryonal carcinoma
c. Yolk sac tumor
d. Choriocarcinoma

e. Teratoma
f. Mixed germ cell tumor
g. Germ cell tumor with somatic type solid malignancy
h. Germ cell tumor with associated hematolymphoid malignancy

Both clinically and biologically, germ cell tumors of the mediastinum are separated into pre- and postpubertalentities. While prepubertal germ cell tumors consists only of teratomas and yolk-sac tumors (either pure-or mixed tumors), postpubertal germ cell tumorscan be of any of the histological type of germ cell tumors seen in gonads with exception of spermatocytic seminomas.

For therapeutic purposes, germ cell tumors are grouped into seminomatous and Non-seminomatous germ cell tumors (NSGCTs) which include yolk sac tumors, embryonal carcinomas, choriocarcinomas, teratomas and mixed germ cell tumors.

**(a)Seminoma**

Seminoma is a malignant neoplasm composed of cells resembling primordial germ cells. Histological features of neoplastic cells includes prominent nucleoli and clear cytoplasm with distinct cytoplasmic borders, fibrous septa, and a dense inflammatory infiltrate comprising a combination of lymphocytes and granulomatous inflammation that may obscure the underlying neoplasm.

Cytology of Seminoma shows dispersed as well as loose clusters of large cells having rounded nuclei, delicate chromatin, prominent single central nucleolus or several small nucleoli and abundant fragile cytoplasm against atigroid background containing lymphocytes and epithelioid cell granulomas. On IHC they are positive for OCT3/4 and SALL4. AFP is negative.

**(b)Embryonal carcinoma** is an invasive, highly necrotic neoplasm. Embryonal carcinoma appears more pleomorphic than seminoma. The histological pattern is variable and within a single tumor there may be solid, papillary, glandular or tubular components. In general tumor cells

are relatively large, polygonal with round or oval nuclei, distinct nucleoli and pale staining cytoplasm with indistinct cell borders. The tumor can be associated with necrosis.

On cytology, smears are usually cellular and are composed of malignant cells arranged in three-dimensional clusters or flat sheets and can form papillary structures or acini. The nuclei are large and pleomorphic with coarse chromatin and prominent nucleoli.

Immunohistochemically, there is reactivity for keratin, PLAP, OCT3/4, SALL4, CD30.

**(c)Yolk sac tumor**

It is the second most common mediastinal germ cell tumor in children less than 15 years of age; yolk sac elements are more common in mediastinal than in testicular neoplasms.[32]

On cytology, smears show aggregates of medium to large cells with variable nuclei, prominent nucleoli, moderate to occasionally abundant cytoplasm and variable background of debris and mucoid or metachromatic material. Lymphoid cells and granulomas are typically not present. Cytological diagnosis should always be correlated with clinical and radiological studies.

On histology, wide spectrum of pattern occurs: microcystic, macrocystic, glandular, pseudopapillary and spindle. Presence of extracellular stringy hyaline material has been reported in yolk sac tumors.[33]Pure yolk sac tumors may occur in the prepubertal testis, but they often occur with other elements as a mixed malignant germ cell tumor in postpubertal patients.

OCT3/4–, SALL4+ immunophenotype help in confirming the diagnosis, especially when combined with staining for alpha-fetoprotein and glypican-3.[34]

**(d)Choriocarcinoma**

It is a highly malignant trophoblastic neoplasm composed of syncytiotrophoblast, cytotrophoblast, and variable intermediate

trophoblast. It is most commonly accompanied by elevated serum levels of human chorionic gonadotropin (hCG).

On cytology there are large areas of hemorrhage and necrosis with a rim of multinucleated large atypical cells, the syncytiotrophoblasts are multinucleated very large cells with eosinophilic cytoplasm one to several nuclei and distinct nucleoli. Mononucleated cytotrophoblasts are medium sized cells with vacuolated, basophilic cytoplasm and eccentric nuclei.

On IHC, they express keratins and are negative for OCT3/4, PLAP, AFP, CEA, CD30 and vimentin. The syncytiotrophoblastic cells express Hcg, glypican 3 and inhibin alpha while mononucleate trophoblastic cells are often positive for SALL4.

**(e)Mature cystic teratoma:**

It accounts for the majority of mediastinal germ cell tumors in children.[35]

Microscopically, the cysts are lined by stratified squamous epithelium and contain sebaceous glands and hair follicles.

Other common components are neural tissue, gastrointestinal tract, cartilage, and respiratory structures. Pancreatic tissue is particularly frequent in this location and may be accompanied by islet cell elements and result in hypoglycemia.

Cytolologic features of teratoma are keratinous debris, squamous epithelial cells, glandular epithelium with hair shaft material. Fine needle aspiration can be difficult because sampling may occur in areas that may not yield as many cells, especially when sampling keratin debris, bone or calcified elements

**Immature teratoma** is defined as a germ cell tumor similar to mature teratoma but also containing immature epithelial, mesenchymal, or neural elements without a component of embryonal carcinoma.

Cytological smears of immature teratomas may be cellular and shows small blue cell tumor. Tumor cells may be isolated or grouped in small aggregates forming branching sheets. The cells have small round, hyperchromatic nuclei with inconspicuous nucleoli and high N/C ratio. Rosettes with neuropil, immature cartilage, blastema like stromal cells are rarely seen.

**(f)Mixed Germ Cell Tumors**

They are characterized by a combination of embryonal carcinoma and teratoma (mature and/or immature), and comprises about 5% of all mediastinal germ cell tumors.

Grossly, areas of hemorrhage and necrosis are present. Microscopically, areas of embryonal carcinoma alternate with foci of predominantly mature teratoma.

Cytological diagnosis of mixed germ cell tumor is difficult as only one element is present. The cytomorphological features of germ cell components are similar to pure germ cell tumors. Cytological diagnosis should always be correlated with clinical, serological and radiological studies.

**LYMPHOMAS:**

Lymphoma is the most common malignant neoplasm involving the mediastinum and accounts for 50-60% of all mediastinal malignancies. Of those, around 65% are Non-Hodgkin lymphomas (NHL). Approximately 10% are primary mediastinal lymphomas thought to arise from the thymus whereas most are secondary lymphomas that involve the mediastinal lymph nodes as part of the systemic disease. Mediastinal lymphomas may involve the thymus, mediastinal lymph nodes, and/or mediastinal organs (i.e. lungs/pleura, heart/pericardium).

**WHO Classification of Lymphomas of the mediastinum (2015)** [36]

i. Primary mediastinal large B-cell Lymphoma
ii. MALT Lymphoma
iii. Other mature B- cell Lymphoma
iv. T Lymphoblastic Leukemia/ Lymphoma
v. Anaplastic large cell Lymphoma(ALCL)
vi. Hodgkin Lymphoma

**Primary Mediastinal (Thymic) Large B-Cell Lymphoma (PMBL)**

PMBL accounts for 2-3% of all NHLs and is the second most common NHL arising in the anterior mediastinum (after T-lymphoblastic lymphoma).[37] PMBL is more common in women and mainly affects young individuals between 20 to 50 years old. The tumor tends to infiltrate local structures including the lungs, pleura, large vessels, chest wall, and diaphragm; however, mediastinal lymphadenopathy is not typically seen, and most patients have localized disease.

On histology, PMBL shows a diffuse infiltrate of atypical lymphoid cells that is almost always associated with sclerosis, which can be in the form of broad fibrous bands or, more commonly, thin bands of compartmentalizing fibrosis separating tumor cells into small nests.

The cytomorphology of the lymphoma cells varies widely from case to case but is usually uniform within a case: the cells can be large with lobated nuclei and clear cytoplasm (due to retraction artifact), may resemble centroblasts or immunoblasts, or rarely may exhibit anaplastic features.

IHC: Tumor cells are positive for CD45 and pan-B-cell antigens (CD20, CD79a, PAX5), typically express CD23, BCL6 and MUM1, and most cases express some amount of CD30, though staining is usually weaker and more variable compared to CHL.[38]

**Thymic Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT)**

Thymic MALT lymphoma is rare, with around only 30 reported cases.[39] The presenting age ranges from 23-75 years old (median 63 years). Over 75% of patients have a history of autoimmune disease, especially Sjögren syndrome (>50% of cases).[40] Thymic MALT lymphomas typically present as large mediastinal masses (mean 9 cm)[41] that are often solid and cystic and confined to thymus without lymphadenopathy.[42]A subset of patients have hyperglobulinemia (usually IgA) with elevated serum M protein levels.[43]

On cytology, the neoplastic infiltrate is polymorphous and composed of small lymphocytes, monocytoid lymphoid cells with clear cytoplasm, plasmacytoid lymphocytes, many mature-appearing plasma cells, and few scattered centroblasts or immunoblasts

IHC: Tumor cells express B-cell specific markers, such as CD20 and CD79a. They are negative for CD3, CD5, CD1, CD23, CD43 and cyclin D1. They commonly express Bcl2, and >70% of the cases express IgA.

**T-Lymphoblastic Lymphoma (T-LBL)**

T-LBL comprises 80-90% of all anterior mediastinal NHLs and 40% of childhood lymphomas.[44] The affected populations are primarily adolescent or young adult males, but older adults can be affected as well. T-LBL typically presents with a large mediastinal mass, though peripheral lymphadenopathy is common and seen in approximately 40% of cases.[45]

On cytology, T-LBL shows a diffuse infiltrate of lymphoblasts, which are immature-appearing lymphoid cells with round or irregular, convoluted nuclei, finely dispersed chromatin, inconspicuous nucleoli, scant cytoplasm, and frequent mitoses. Lymphoblasts are medium-sized in most cases, approaching the size of histiocyte nucleus, though some cases contain smaller nuclei with variably condensed chromatin resembling mature lymphocytes.

IHC: CD3 expression along with variable expression of CD2, CD7, CD5, CD1a, CD4 and or CD8 and CD10.

**Hodgkins Lymphoma**

Hodgkin's lymphoma is a lymphoma of B cell origin. The two major types are classical Hodgkin lymphoma and nodular lymphocyte-predominant Hodgkin lymphoma. The four subtypes of classic Hodgkins lymphoma (HL), based on the Reed-Sternberg cell morphology and the type of infiltrate on biopsy, are nodular sclerosis, lymphocyte-rich, mixed cellularity, and lymphocyte-depleted. The most common type of Hodgkin's lymphoma is nodular sclerosis classical Hodgkin lymphoma[46] has a predilection for the thymus.

**Nodular Sclerosis Classic Hodgkin Lymphoma (NSCHL)**

NSCHL accounts for 70% of all classic Hodgkin lymphomas (CHLs) in the United States and Europe and most commonly presents in young females aged 15-34 years.[47] It comprises approximately 35% of all mediastinal lymphomas, with about half of cases arising in the thymus,[48] while the remainder represent secondary involvement of mediastinal lymph nodes. Of all NSCHLs, mediastinal involvement in seen in 80% of cases, with presentation as a bulky mass (defined as ≥7 cm in greatest dimension) in 54% of cases.[49] The other subtypes of CHL usually involve peripheral lymph nodes and are not typically seen in the mediastinum.[50]

On cytology, smears are predominantly composed of a reactive mixed inflammatory background consisting of small lymphocytes, neutrophils, histiocytes, plasma cells, and notably eosinophils. The neoplastic Hodgkin/ReedSternberg (HRS) cells comprise only a minority of the total cell population and are classically large, atypical mononuclear or binucleated cells with prominent central eosinophilic macronucleoli, perinucleolar clearing and abundant amphophilic cytoplasm.

Patients with Hodgkins lymphoma experience B symptoms (fevers, night sweats, and weight loss), and patients with mediastinal

involvement may develop chest pain, cough, and shortness of breath. Involvement of local structures may result in SVC syndrome.

On IHC, classical HL are CD30 and CD15 positive. PAX5 is expressed more weakly in RS cells than in normal B cells.

**Lipoma**

Lipomas are rare tumors in the mediastinum but they are common benign tumors among mesencymaltumors. Histologically mediastinal lipomas are identical to their cutaneous and soft tissue counterparts seen as well encapsulated tumor composed of mature adipocytes with small eccentric nuclei.

**Lesions in Superior Mediastinum**

**Parathyroid Adenoma**

Approximately 10-20% of parthyroid neoplasms occur in the mediastinum, most commonly in the anterosuperior mediastinum .Parathyroid adenomas are circumscribed tumors that consist of sheets and trabeculae of polygonal cells traversed by a delicate vasculature. There is mixture of cells with clear, eosinophilic, amphophilic or oxyphilic cytoplasm. The nuclei are uniform and round.

Cytologically, aspirates are cellular with uniform small cells in sheets, three dimensional clusters and trabecular arrangements with round nuclei with smooth nuclear borders without nucleoli

**Mediastinal Goitre**

Mediastinal goitre generally represents direct contiguous growth of a goitre into the anterior or superior mediastinum. Typical features of mediastinal goitres are encapsulated and lobulated mass with homogeneous appearance with cystic areas, calcifications and marked contrast enhancement. An intrathoracic thyroid mass developing from heterotopic thyroid tissue without any connection to the thyroid in the neck is extremely rare. The presence of ill-defined margins, invasion of adjacent structures and nearby lymph node enlargement suggests the diagnosis of thyroid cancer.

Thymoma and lymphoma are also seen in the superior mediastinum.

**Lesions in Middle Mediastinum**

**Pericardial Cyst**

Itis a benign lesion accounting for 5–10% of all mediastinal tumours[51] Most pericardial cysts are unilocular and commonly located in the right cardiophrenic space. They are lined by single layer of flat or cuboidal mesothelial cells and contain clear, straw colored fluid. They may or may not be attached to the pericardium. On cytology, if is not complicated by inflammation or hemorrhage, the straw colored, sparsely cellular fluid will contain only a few mesothelial cells and mature lymphocytes.

**Bronchogenic Cyst**

Bronchogenic cyst is the most common benign congenital cysts of the mediastinum. It result from abnormal ventral budding or branching of the tracheobronchial tree during embryologic development. They are lined by pseudostratified, ciliated columnar respiratory epithelium that may undergo squamous metaplasia. In the absence of respiratory epithelium, these cysts are recognized by presence of smooth muscle, tracheobronchial glands and sometimes cartilage in the wall. They are stable in size, except when complicated by infection or haemorrhage.

Cytologic diagnosis depends on finding recognizable respiratory epithelium in the usually sparsely cellular fluid aspirate .In the absence of respiratory epithelial cells, we will be able to confirm that a visualized mass is cystic by the nature of fluid aspirated and also by clinical and radiological presentation.

**Lesions in Posterior Mediastinum**

**NEUROGENIC TUMORS**

Neurogenic tumours are derived from tissue of the neural crest, including cells of the peripheral, autonomic, and paraganglionic nervous systems. They are classified on the basis of cell type and comprise approximately 12 to 21% of all mediastinal masses, although 95% occur in the posterior compartment.[52] Ganglioneuromas are

benign tumors composed of one or more mature ganglionic cells. Arising from the nerve ganglion cells they are the most benign and differentiated of the autonomic ganglionic tumors.

**a. Schwannoma**

Schwannoma is a benign nerve sheath tumor composed of a pure neoplastic population of Schwann cells. In some studies it is the most frequent nerve sheath tumor involving the mediastinum.[53]

The cytomorphologic features of schwannoma include smears consisting predominantly of clusters of spindle cells. The clusters are variably cellular but show fibrillary, more commonly than, fibrous stroma; and variably shaped spindled nuclei, chromatin texture is even and fine. The cellular variant may have an increased recurrence risk and demonstrate local destruction, but no metastatic potential.[54]Other rare variants of schwannomas that have also been reported in the mediastinal compartment include plexiform schwannoma and “neuroblastoma-like” schwannoma.[55] The differential diagnosis of deep spindle cell neoplasms which are amenable to fine needle aspiration principally includes leiomyoma, fibromatosis, and gastrointestinal stromal tumor.[56]

**b. Neurofibroma**

Neurofibroma is a benign peripheral nerve sheath tumor which in addition to neoplastic Schwann cells contains a mixture of other cell components, including fibroblasts, mast cells, axons and perineurial cells. On cytology, the neoplastic schwann cells are spindle cells with hyperchromatic wavy nuclei, usually smaller than those of schwannoma, in a myxoid collagenous background. Cytologic atypia can be seen and it is usually of a degenerative nature, lacking prognostic significance. Neurofibromas may also have increased cellularity. Immunohistochemical stains demonstrate strong S100 and SOX10 expression in most. A network of CD34 positive cells is another useful feature. Although the nuclei of neurofibroma are usually smaller in tissue sections, in cytologic preparations neurofibroma and

schwannoma share many features and it may not be possible to distinguish them. On those cases, a cytological diagnosis of benign peripheral nerve tumor is appropriate.[57]

**c. Malignant peripheral nerve sheath tumor (MPNST)**

MPNST may be difficult to differentiate from other high grade spindle cell neoplasms due to lack of specific cytomorphologic features and immunohistochemical profile at first time diagnosis.[58]

The most commonly described cytomorphologic features of MPNST include the following: cellular aspirate, composed predominantly by dispersed spindle cells and or loosely cohesive clusters of neoplastic cells showing mild pleomorphism. However, the proportion of necrosis, fibrosis, and myxoid areas present significantly affects this. Cellular aggregates can show fascicle formation, adjacent necrosis, and even variable amounts of collagen. The cells have high nuclear:cytoplasmic ratio. The spindle nuclei can be wavy, buckled or smooth.[59] Chromatin is typically evenly dispersed and granular, and macronucleoli absent or exceedingly rare. The presence of mitoses, pleomorphism and necrosis are most helpful in the differential diagnosis with benign precursors (e.g. neurofibroma), but highly non-specific findings in the differential diagnosis with spindle cell malignancies.

**d. Ganglioneuroma and Ganglioneuroblastoma**

**Ganglioneuroma**

It is a slow growing neoplasm with benign Schwann cell and ganglion cell components. The patients are usually asymptomatic at presentation. Ganglioneuroma comprises up to 35% of intrathoracic neurogenic tumors.[60] Ganglioneuromas are most often diagnosed in younger patients, with most patients presenting before the age of 20.[61]

FNA of ganglioneuromas result in low to moderate cellularity smears with two distinct elements: scattered, mature ganglion cells and spindled Schwannian stroma. Ganglion cells, when present, are easily identified by their abundant granular cytoplasm, eccentrically placed large nuclei, and prominent nucleoli. The Schwannian stroma is

characterized by its elongated, wavy, uniform nuclei and fibrillary, ill-defined cytoplasm. When both ganglion cells and Schwannian stroma are present in FNA material, without the immature neuroblastic elements of ganglioneuroblastoma, the diagnosis of ganglioneuroma is relatively straightforward. On IHC both the ganglion cells and schwannian stroma stain positively for S100 and neuron-specific enolase (NSE), and are negative for cytokeratins. Synaptophysin and neurofilament protein strongly label the ganglion cells.

**Ganglioneuroblastoma**

Ganglioneuroblastomas are characteristically seen in younger patients than ganglioneuromas [62] and metastases are evident at presentation in a substantial number of cases.[63] Ganglioneuroblastomas are generally grouped together with neuroblastomas for the purposes of cancer staging and prognosis.[64] Microscopically, FNA of ganglioneuroblastomas results in cellular smears with three distinct elements: mature ganglion cells (as seen in ganglioneuroma), abundant immature neuroblasts, and variable amounts of Schwannian stroma. Neuroblasts have the characteristic appearance of small round blue cells, often with associated neuropil (which appears finely granular and homogenous). Homer-Wright rosettes (circular arrangements of neuroblasts with a central core of neuropil) are typical of both ganglioneuroblastoma and neuroblastomas, but are not always present.[65] Additional high grade features such as high mitotic rate, karyorrhexis, and necrosis may be present.

**e. Paraganglioma**

Paraganglioma of the mediastinum is a rare neoplasm, comprising <1% of mediastinal tumors.[66] Fine needle aspiration smears shows bloody, hypercellular smears with groups or dyscohesive groups of polygonal cells intermixed with fat and blood vessels. Nuclei are typically bland but frequently show anisonucleosis with few to no mitotic figures. Naked nuclei are common but the cytoplasm is typically abundant and can show granularity with fine red granules.[67] On IHC

paragangliomas are characteristically keratin negative, neuroendocrine marker positive, and express GATA3.

**Gastroenteric cysts**

These are located in the posterior mediastinum and are lined by gastric or intestinal mucosa. The Mucosa does not easily shed recognizable glandular cells and such cells are dislodged by neddle.

**INFLAMMATORY CONDITIONS:**

**Acute mediastinitis**- occurs due to traumatic perforation of esophagus or descent of infection from within the neck through danger space. It predominantly involves the posterior portion of the mediastinum.[68] Abscess formation usually takes place and generally requires surgical drainage.

**Chronic mediastinitis**- produces compression of mediastinal structures and mimics malignancy.[69] It typically involves the anterior mediastinum.It includes granulomatous mediastinitis, fibrosing mediastinitis or a combination of both.

**Sarcoidosis-** Sarcoidosis is a multi-system disease of unknown etiology, usually affecting the respiratory tract and other organs, and characterized by the formation of nonnecrotizing epithelioid granulomas. Sarcoidosis is a clinicopathologic diagnosis, and it remains a diagnosis of exclusion of other conditions that can produce similar granulomas. Currently, the diagnosis of sarcoidosis depends on a combination of three different features: a typical clinico-radiological presentation; the histologic presence of nonnecrotizing epithelioid granulomas in a tissue biopsy; and exclusion of other possible diseases, especially those of infectious etiology, which may produce nonnecrotizing or minimally necrotizing granulomas.

The epithelioid granuloma has been defined as a compact (organized) collection of mature mononuclear phagocytes (macrophages and/or epithelioid cells). Multinucleated Langhans-type giant cells, resulting from fusion of epithelioid mononuclear cells, are often seen in the

granulomas. These granulomas show CD4+ T cells in their center and a cuff of CD8+ T lymphocytes and B lymphocytes at their periphery.[70] Sarcoid granulomas are immune granulomas resulting from a specific cell-mediated response to unidentified antigenic agent/agents. Many of the granulomas are nonnecrotizing, but small foci of central fibrinoid, granular, or eosinophilic necrosis are not unusual.

A number of nonspecific cytoplasmic structures/inclusions can be identified within the granulomas of sarcoidosis. Asteroid bodies are star-shaped spiculated structures that typically occur within multinucleated giant cells. They are seen in only 2% to 9% of sarcoidal granulomas.[71]

Schaumann's bodies, or conchoidal bodies, consist of small calcifications with a lamellar morphology. They occur in 48% to 88% cases of sarcoidosis.

**INFECTIONS**

Among nonneoplastic conditions, tuberculosis was the most common lesion (20.1%).[19] The cytological features in tuberculosis include epithelioid granulomas. These are activated macrophages with elongated plump nuclei having fine nuclear chromatin, inconspicuous nucleoli and scant cytoplasm. The nuclei are drawn out or folded giving a slipper like shape. Langhans giant cells are characteristic feature of tuberculosis. These are 2-10 times the size of mononuclear macrophages and may even contain upto 100 nuclei and nuclei are placed towards one pole of the cell resembling horse shoe shape. Epithelioid cell granulomas are seen in FNA material. Pale amorphous material often suggests caseation necrosis. Tubercle bacilli are most likely to be found within the caseous necrosis. In the FNAC tubercle bacilli are demonstrated by staining with 20% Ziehl-Nielsen (ZN) stain and they are seen as beaded magenta straight or slightly curved acid fast bacilli

**Nina S. Shabb et al**[72] **studied** Forty-two fine-needle aspirates (FNA) of the mediastinum from 1984–1995. There were 25 males and 17

females with age range from 10–72 yr and a mean age of 41 yr. The most common symptoms were dyspnea, cough, and chest pain. 6 were asymptomatic from their mediastinal lesion and were discovered by routine chest X-rays. 38 of the aspirated tumors were in the anterior or anterior/superior mediastinum, while only 4 were in the posterior mediastinum. The majority of the tumors were solid, some were mixed solid and cystic, and a few cases were purely cystic. 7 tumors had invaded the chest wall (mostly lymphomas and one germ-cell tumor). The fine-needle aspirate yielded adequate tissue for diagnosis in 35 of 42 cases (83%). In 7 cases the aspirates were scanty and hence inadequate for diagnosis. This was due to dense fibrosis in the lesion in 2 cases of lymphoma, and due to extensive necrosis in one case of tuberculosis. In 4 cases the cause of the inadequate specimen was not evident but has been related to poor cooperation of the patient, or poor aspirating technique. The majority of cases (57%) were primary neoplasms of the mediastinum which included 7 cases of Hodgkin's lymphoma, 6 of Non-Hodgkin's lymphoma out of which 4 of large-cell lymphoma (LCL), and 2 of lymphoblastic lymphoma (LL); 3 of thymoma, 3 of germ-cell tumor, thymic carcinoid and angiosarcoma, 1 each; and 3 of malignant not otherwise specified. Twenty-four percent were metastatic tumors 9 of carcinoma and 1 of sarcoma. Twelve percent were benign conditions which included 2 cases of granulomatous disease, 1 of multinodular goiter, 1of extramedullary hematopoesis and one thymic cyst. Seven percent were inconclusive. FNA yielded adequate tissue for diagnosis in 83% and a correct diagnosis in 86%.

**Margaret W Assaad** et al[73] conducted a retrospective study of 157 consecutive CT-guided transthoracic FNAB of the mediastinum from 1988 to 2004. Patients were of average age 57 yr (range 1-88 yr), including 75 males and 82 females. A definitive diagnosis was rendered in 128 (82%) cases. Primary neoplasms (N = 38) included 24 lymphomas (6 Hodgkin and 18 non-Hodgkin), 7 thymomas, 1 thymic carcinoma, and 6 peripheral nerve sheath tumors. Metastases (N = 72)

were mainly carcinomas (N = 71) and 1 melanoma. There were 4 non-neoplastic lesions (1 granulomatous process; 2 bronchogenic and 1 pericardial cyst), 1 case of undifferentiated malignant large cell neoplasm, 13 cases negative for malignancy, and 29 (18%) that were indeterminate, largely due to insufficient cellularity. Adequate diagnostic cytologic material was obtained by image-guided percutaneous FNAB of mediastinal lesions in 82% of our cases. Therefore, percutaneous FNAB of the mediastinum is a diagnostically helpful, minimally invasive procedure that can be performed in patients of all ages as part of the evaluation of a mediastinal mass lesion.

**D. K. Pandey et al**[74] studied a total of 56 patients having mediastinal mass with or without lung lesions from March 2000 to March 2002. Of these patients, 36 had mediastinal mass only and 20 had mediastinal mass with parenchymal lesion. Maximum numberof cases were in the age group of 51-60 years with a mean age of 52 years. Male preponderance of 85.7% was seen. About 66.1% of total cases were malignant and 19.6% were benign. Out of 12 benign lesions, non specific inflammation was found in 2 cases and specific inflammation in 5 cases. 1 case is of mediastinal cyst, 2 of retrosternal thyroid, 1 of reactive change of lymph node and 1 of cystic teratoma. FNAC was inconclusive in 8 (14.3%) cases. 36 cases were neoplastic in nature. Malignant lesions were cytologically characterized as 28 cases of carcinoma (50%), 7 of lymphoma (12.5%) and 1 of primitive neuroectodermal tumor (1.8%). On cell typing, it was found to have 9 cases of squamous cell carcinoma, 7 of adenocarcinoma, 1 of brochoalveolar carcinoma, 10 of small cell carcinoma and 1 of poorly differentiated carcinoma. There were 5 cases of Non-Hodgkin's lymphoma and 2 cases of Hodgkin Lymphoma.

**Deepa Goel et al**[75] done a retrospective study of mediastinal lesions that were referred for ultrasonographic/computed tomography–guided FNAC during the years January 2001 and December 2006. The total number of patients was 161. There were 107 male and 54 female

patients (M/F ratio, 2:1), with 15 children under age 15 years. Material was adequate for diagnosis in 130 (81.8%) cases. There were 28 nonneoplastic lesions and 102 neoplastic lesions; in 31 (19.2%) cases, material was unsatisfactory for evaluation out of 28 (21.5%) nonneoplastic cases, 18 (64.3%) were inflammatory. 15 were of tuberculous etiology, and caseous necrosis was noted in 8; however, stain for acid-fast bacilli (AFB) was negative in all. 1 patient was diagnosed as having aspergillosis based on the presence of thin, septate, acute-angle branching hyphae on Gomori's silver methenamine (GSM) staining.1 patient had suppurative inflammation with neutrophils, and the smears were negative for AFB and fungi. 1 patient had noncaseating granulomatous inflammation, and was diagnosed as sarcoidosis based on clinical features and response to treatment. There were 4 benign cysts. In addition, 1 case each of thymic hyperplasia and ectopic thyroid. Four cases were labeled as negative for malignancy. Of 130 cases, 102 (78.5%) were neoplastic lesions. These included benign and malignant tumors. Lymphomas constituted 27 of 102 (26.5%) lesions. Non-Hodgkin's lymphomas were 23 out of 27 (85.1%). 19 were adolescents and showed lymphoblastic lymphoma on aspirates. 4 cases were of large cell type. There were 4 cases of Hodgkin's lymphomas. Thymomas accounted for 13 out of 102 (12.7%) cases. 7 (6.9%) cases of germ cell tumors which includes 4 yolk sac tumors and 1 each of seminoma, mature teratoma and choriocarcinoma. The most commonly found malignant lesion was carcinoma, with 32 (31.4%) cases. 8 (7.8%) neurogenic lesions were located in the posterior mediastinum including 5 schwannomas, 2 neuroblastomas, 1 paraganglioma. Sarcomas accounted for 3 of 102 (2.9%) lesions.

**Tin Q. Nguyen et al**[76] conducted a retrospective study on one hundred forty-eight patients who underwent mediastinal EUS FNAC at St Vincent's Hospital between February 2002 and August 2007. Males comprised 63.5% (n = 94). The mean age of patients was 64.3 (range 27–85). Full data was available on 124 of 148 (83.8%) cases, as 14

cases had no available comparative final histologic and/or clinical data, and results were unknown in the remaining 10 cases. Of the 124 mediastinal EUS cases, 112 underwent FNA. Of the patients that had FNA, a positive diagnostic FNA was found in 77.7% (87/112) of cases; 86.2% (75/87) of these had malignant histology, with NSCLC as the most common diagnosis. There were 9 cases of metastatic disease, with primary sites from skin (2), breast (1), prostate (1), colon (1), adrenal (1) and neuroendocrine origin (3). There were 4 cases of lymphoma, 1 of small cell carcinoma and the remaining had malignancy of unspecified histologic cell type. The remaining positive FNA cases (13.8%; 12/87) had non malignant histology. There were 11 cases of sarcoidosis and one case of tuberculosis. Some cases (25/112; 22.3%) had a negative FNA

**Alan Marcus et al**[77] studied 107 patients with mediastinal masses from 2006 and 2015. The age range of the 107 patients with mediastinal FNAC was 7 to 88 years old of which 38.3% were males and 61.7% were females. They were all biopsied using some form of guidance: Transthoracic Computed Tomography (CT) (92), Endobronchial Ultrasound (14), and Endoscopic Ultrasound (1). Tumors were located respectively in the anterosuperior mediastinum (65), posterior mediastinum (6), middle mediastinum (2), and mediastinum, not otherwise specified (NOS) (34). The final diagnoses of the 107 FNAC specimens and the 77 surgical pathology specimens were infectious/inflammatory (7,6), metastatic carcinoma (24,15), lymphoma (20,19), cysts (6,4), soft tissue tumors (5,3), paragangliomas (2,2), germ cell tumors (2,2), thymoma (20,15), thymic carcinoma (6,5), benign thymus (2,1), indeterminate (12,5), and benign thyroid (1,0). The overall sensitivity for mediastinal mass FNAC was 78% and the overall specificity was 98%. The sensitivity and specificity of FNAC in the individual categories were inflammatory/ infectious (33%, 99%), metastatic carcinoma (93%, 100%), lymphoma (84%, 97%), cyst (25%, 100%), soft tissue tumor (100%, 100%), paraganglioma (50%, 100%), germ cell tumor (100%, 99%), thymoma

(87%, 94%), thymic carcinoma (60%, 100%), benign thymus (0%, 100%), and indeterminate (100%, 90%)

**Jitendra G et al.**[78] conducted a prospective study over a 3-year period from 2008 to 2011 of 50 patients who underwent CNB and FNAC for their anterior mediastinal masses. Among 50 patients, there were 36 male and 14 female with the mean age of 38.6 years (range 1-76 years). The male to female ratio was 2.5:1. Metastatic carcinoma remains the most common entity followed by nonHodgkin's lymphoma (NHL). One case had unsatisfactory material to evaluate both cyto-histological features. The rest 49 cases were divided into carcinoma and noncarcinoma group. The proportion of noncarcinoma group is more (27 cases; 55.10%) as compared with carcinoma group (22 cases; 44.89%). Carcinoma group composed of metastatic adenopathy of the mediastinal nodes (18), small cell lung cancer (2), and neuroendocrine carcinoma (1). In noncarcinomatous group, tumors include NHL (16), Hodgkin's lymphoma (01), thymoma (6), thymolipoma (1), germ cell tumor (2), and carcinoid tumor (1).

**Usha R Dalal et al**[79], conducted a study over a span of 11 years (2008-2019) in which they studied 29 adult patients with mediastinal masses. Of these 29 patients 15 (51.7%) were males and 14 (49.3%) were females. Age range was from 18to 75 years of age with mean age of 33.6 years and median of 30years. Benign pathologies dominated with28 out of 29 being benign masses (96.5%), and only a single case turned out to be malignant (3.5%). 17 masses (58.6%) were localised to anterior mediastinum and 9 (31%) were localised to posterior mediastinum. Only 3 cases (10.3%) were localised to the middle mediastinum. Out of 6 cases of Thymoma 5 turned out to be benign and 1 turned out to be a case of aggressive malignant thymic carcinoma, there were 5 cases of neurofibroma, 2 cases of schwannoma and 1 case of ganglioneuroma. 3 cases were of retrosternal goitre, 6 cases of teratomas, all of them were mature.

**Senjuti Dasguptaet al.**[5] conducted a retrospective study of 22 cases presenting with mediastinal masses between May 2011 and April 2014. Of the 22 patients included, 15 were males and 7 were females. The male to female ratio was 2:1. Their age ranged from 6 months to 56 years. The mean age of the patients was 18° 3 years.
In this, 10 (45.5%) tumors were found in the anterior mediastinum, 7 (31.8%) in the middle mediastinum, and 5 (22.7%) in the posterior mediastinum. CT-guided FNAC was done in 15 cases. These included 4 cases of thymic lesions, 3 of extra gonadal GCT, 5 of lymphoma, 2 of schwannoma, and one case of ganglioneuroma. .Among the 5 cases of lymphoma, 3 were found to be CD 15 and CD 30 positive and they were diagnosed as Hodgkin lymphoma. A diagnosis of T-cell lymphoma was given in the other 2 cases as they furnished positive results with CD 3, Tdt, and CD 34 immunostains. One case of mixed GCT was diagnosed, and it consisted of components of yolk sac tumor and dysgerminoma. Among the other 2 cases of GCT, one was microscopically found to be a case of mature cystic teratoma and the other, dysgerminoma.

**Preeti Sharma et al**.[80] conducted a retrospective study from January 2011 till January 2016 in which they studied 60 cases of mediastinal lesions in which 22 were anterior, 20 were middle and 18 posterior mediastinal masses. There were 43 males and 21 females with a male: female ratio of 2:1. The mean patient age at the time of presentation was 37.5 years (range 2-61 years).The majority of the patients were symptomatic (96.8%). The most common presenting complaint was cough, seen in 54 patients (87.0%), followed by chest pain (50; 80.6%), weight loss (36; 58.0%), dyspnoea (26; 41.9%) and hoarseness (14; 22.5%). FNAC was done in 54 cases of which 7 cases yielded inadequate material. The most common pathology was thymoma (12 cases) followed by ten cases of lymphoma, eight cases each of tubercular lymphadenopathy and schwannoma, six cases of neurofibroma, four cases of extragonadal germ cell tumours, two cases each of thymic cyst, bronchogenic cyst, retrosternal goitre,

ganglioneuroma and neuroblastoma, and one case each of lipoma and thymolipoma.

**Ananya Choudhuri et al**[81]**,** done aretrospective study of 25patients, who had undergone diagnostic evaluation by imaging modalities between 2013 and 2018. Among 25 cases, cytological features were adequate to establish the diagnosis in 23 cases. There were eighteen males and seven females with a male to female ratio of 2.6:1.out of 25 cases, 24 patients (96%) were symptomatic at the time of presentation, cough being the prominent symptom seen in twenty patients (83.3%) followed by chest pain in eighteen patients (75%), shortness of breath in fifteen patients (62.5%). Out of 25 cases, seventeen cases (68%) were malignant, six cases (24%) were benign or inflammatory lesions, and two cases (8%) were inadequate to establish any diagnosis.

Out of the six inflammatory and benign cases, four had biopsy correlation, which confirmed the FNAC diagnoses including one case each of thymoma and schwannoma. Out of ten malignant cases, CNB was done in five cases including one case each of metastatic squamous cell carcinoma, metastatic adenocarcinoma, germ cell tumor, which was confirmed as mediastinal seminoma, and poorly differentiated carcinoma, which was confirmed as thymic carcinoma. Complete excisional biopsy was done in one case of a small round cell tumor, which was confirmed as Ewing's sarcoma. Two cases of non-Hodgkin's lymphoma had flow cytometry done on FNAC aspirates along with CNB correlation. There were two inconclusive cases on FNAC, which did not have any histopathological or cell block correlation.

Another study by **Sakthisankari Shanmuga Sundaram et al.**[82] conducted a retrospective study on all mediastinal masses over a period of two years from January 2016 to December 2018. Thirty four cases of mediastinal lesions were included. Majority of the lesions were females with male to female ratio being 1:1.5. Age of the patients ranged from 14 to 75 years. About twenty eight (82.4%) cases

presented as anterior mediastinal masses, and three cases each in the middle and posterior mediastinum. Thymoma (n=15) followed by lymphoma (n=4) were the most frequent neoplasms reported. There were five lesions which were rare in the mediastinum with unusual presentation. These lesions included Primitive neuroectodermal tumour in an adult, Primary Mediastinal B Cell Lymphoma (PMBCL), Malignant Peripheral Nerve Sheath Tumour (MPNST) with nodal metastasis, Seminoma deposits in mediastinal node occurring as late relapse and dedifferentiation of thyroid carcinoma in mediastinal node metastasis without an obvious primary.

**Mohamed S. AbdelrahmanHantera** et al[83] carried out a retrospective analysis of ninety two patients with mediastinal lesions during the period of 2017–2018.

The majority of patients were men (69 men and 23 women) and the age ranged from 18 to 66 years, mean±SD 46.03±15.08. The most frequent pathological finding was lymphomas, 34.78%, followed by adenocarcinomas, 26%; other findings included sarcoidosis (17.39%), small cell carcinoma (4.34%), seminomas (3.26%), thymomas (3.26%), retrosternal goiter (2.17%), and neurofibroma (2.17%), and 1.08% each of tuberculosis, sarcoma, large cell carcinoma, thymic carcinoma, carcinoid tumor of the thymus, and undifferentiated thymic tumor

Another study by **Ramakant Dixit et al**[84] studied 144 patients over the last 8 years Five cases were not included in this as their diagnosis was confirmed on the CT scan thorax and not requiring invasive diagnostic workup by FNAC/core biopsy. The age range of the patients was between 14 and 76 years, with a mean age of 45.5 years. 116 were male and 23 patients were female, with a male to female ratio of 5:1. The mean duration of symptom was 110 days (range: 16–810 days) There were 95 cases (68.3%) confined to the anterior mediastinum, 23 cases (16.5%) to the middle, and 11 cases (2.5%) to the posterior mediastinum. In 10 cases (7.1%), two or more than two compartments of the mediastinum were simultaneously affected. Out of 139 cases, 93

cases were neoplastic in nature (67%), 32 were nonneoplastic (23%), and 14 remained inconclusive (10%). Among neoplastic mediastinal lesions, metastatic carcinoma (37.4%) was the most common neoplastic lesion, followed by Non-Hodgkin's lymphoma (12.2%), Hodgkin's lymphoma (7.1%), thymic lesions (3.5%), etc. Among nonneoplastic conditions, tuberculosis was the most common lesion (20.1%).

**Akshatha Rao Aroor et al**[85]conducted a prospective study over a period of 2 yearsin which they studied a total of 35 cases of mediastinal mass, confirmed by CT imaging. The age range affected by mediastinal tumour was between 17 to 68 years, with the mean age of 45.4 years. About 2/3$^{rd}$ of cases (24; 68.57%) were males and 11 cases (31.43%) were females, with a male to female ratio of 2.2:1. About 2/3rd of cases were malignant (24; 68.57%) and benign tumours accounted for eleven cases (31.43%). Among 12 cases of lymphoma, 7 were Hodgkin lymphoma (HL) and 5 cases were Non-Hodgkin Lymphoma (NHL). 4 NHL cases were diffuse large cell B type lymphoma and one case was lymphoblastic lymphoma. Among six cases of thymoma, five were benign. Germ cell tumours were seen in two cases and both were in the anterior mediastinum, of which one was benign mature teratoma and the other was malignant non-seminomatous tumour. Among seven cases of bronchogenic carcinoma, four (57.14 %) were adenocarcinoma, two (28.57%) were squamous cell carcinoma and one (14.29%) was small cell lung carcinoma.

# MATERIALS AND METHODS

This study was conducted in Dayanand Medical College And Hospital, Ludhiana for a period of 5 years from 1st July 2016 to 30th June 2021 (Three and a half years retrospective from 1st July 2016 to 31st December 2019 and one and half years prospective from 1st January 2020 to 30th June 2021) .The smears received in the cytology laboratory from image guided FNAC of mediastinal lesions were analysed and cell blocks were made whenever possible. Relevant special stains were used. During this period all specimens were correlated with clinical and radiological findings & histopathology and IHC was used wherever possible.

A total of 9088 cases of fine needle aspiration cytology were received during the study period. Out of these102 cases were FNAC from mediastinal lesions.

**METHOD OF COLLECTION OF DATA**

**INCLUSION CRITERIA**

FNAC samples from mediastinal lesions received in the Cytology Laboratory of the pathology department which included.

1. FNAC slides received in the department after guided aspiration (ultrasonography and/or CT guidance and/or endoscopic ultrasonography).
2. Prepared and stained slides for review from an outside centre.

**EXCLUSION CRITERIA-**

Samples obtained from lesions other than the mediastinum.

**METHOD OF COLLECTION OF DATA**

After informed consent, USG guided percutaneous fine needle aspiration (FNAC) was done.

**MATERIAL USED**

1. Cameco's syringe pistol
2. Disposable 20 ml syringe

3. Needle 21G/ 23G
4. Glass slides
5. Spirit swab
6. Dry swab / cotton gauge
7. Disposable gloves
8. Diamond pencil for marking slides
9. FNAC reporting form
10. Tray for carrying slides

**PROCEDURE DONE**

Radiologically guided percutaneous fine needle aspiration (FNAC) was done using 21 guage spinal needle for mediastinal masses attached to 20cc disposable plastic syringe. Taking aseptic precautions, needle was introduced in suspended respiration, slides were prepared immediately. One of the slide was utilized for rapid on site evaluation for adequacy by the Toulidine Blue stain. Two of them were wet fixed in 95% ethanol and stained with Papanicolaou stain and Hematoxylin and Eosin. The remaining smears were air dried and stained by May Grunwald Giemsa stain.

FNA sample was collected in a separate pass and fixed in 10% formalin, processed and embedded to make a cell block. Sections were stained byH & E stain. Special stains were done wherever necessary Cytopathological-histopathological correlation was done wherever possible.

The smears obtained by FNA (ultrasound/CT guided) of all mediastinal masses were analysed in this study and categorized. The cytological findings were correlated with the clinico-radiological profile, histopathological findings, special stains and IHC findings wherever possible.

**Staining of smear**

1. Dry fixed smears were prepared by air drying and then fixing inmethanol followed by staining with Giemsa

2. Wet-fixed smears were prepared by immediately fixing in 95% isopropyl alcohol and stained by H & E and Papanicolaou stain.

**Giemsa Stain:**

Giemsa stock

Geimsa stain powder 4 gm

Glycerol 250ml

Methanol 250ml

Giemsa working solution

Giemsa 4ml

Distilled water 96ml

Procedure:

1. Smears were air dried and fixed with methanol.
2. Giemsa stain 1 in 10 dilutions (9ml water, 1ml Geimsa stain) waspoured over the slides to cover whole of the smear for 10 minutes.
3. Stain was removed and slides washed with distilled water thoroughly and air dried.
4. Mounting in DPX.

**Hematoxylin & eosin**

Stain solutions: Harris's Hematoxylin

Hematoxylin 2.5 gm

Absolute alcohol 25ml

Potassium alum 50 gm

Distilled water 500 ml

Mercuric oxide 1.25 gm or

Sodium iodate 0.5gm

Glacial acetic acid 20ml

Eosin 1% (commercially available)

95% Ethyl alcohol

Acid alcohol

1% Ammonia

Acetone

Xylene

1) The smears were fixed with 95% rectified spirit or ethyl alcohol and kept for ½ hour.

2) Then ten dips each were given in 80%, 70%, 50% alcohol.

3) Washed in distilled water-10 dips.

4) Harris hematoxylin- 3 mins.

5) Washed in running tap water till excess stain was removed - 1 min.

6) Acid alcohol 0.5% HCl -10 dips.

7) Washed in running tap water- 30 secs.

8) 1% ammonia -3 dips

9) 95% alcohol -10 dips.

10) Eosin - 20 dips

11) Acetone -10 dips

12) Acetone - 10 dips

13) Xylene -10 dips

14) Xylene -10 dips

**Papanicolau Stain requirements**

Stain Solutions:

Harris Haematoxylin

| | | | |
|---|---|---|---|
| Hematoxylin | 2.5gm | Distilled water | 500ml |
| Mercuric oxide | 1.25 gm or | Absolute alcohol | 25 ml |
| Sodium iodate | 0.5 gm | Potassium alum | 50 gm |
| Glacial acetic acid | 20 ml | | |

Orange G 6

| | |
|---|---|
| 10% aqueous Orange G | 50 ML |
| Alcohol | 950 ml |
| Phosphotungstic acid | 15 gm |

Eosin alcohol 36

| | |
|---|---|
| 0.5% light green | 0.5% Eosin |
| 0.5% Bismarck brown | 95% ethyl alcohol |
| Phosphotungistic acid | Glacial acetic acid |
| Lithium carbonate | Absolute methanol |

Procedure-

1) The smears are wet fixed with 95% rectified spirit for half an hour.

2) Then ten dips each were given in 80%, 70%, 50% alcohol.

3) Washed in distilled water. 4) Stained with harris‟s haematoxylin 0-3 mins.

5) Washed in running tap water.

6) Given 10 dips in 1% ammonia.

7) Washed in running tap water.

8) Dipped in 95% alcohol-10 dips.

9) Kept in orange- G 6 for 30 secs.

10) Given 10 dips in 95% and repeated again.

11) Kept Eosin Alcohol 36 for 2 mins. 12) Acetone – 10 dips.

13) Again acetone 10 dips. 14) Xylene – 10 dips. 15) Again xylene – 10 dips.

16) Mounted slide with DPX. Ziehl –Neelsen (ZN) stain requirements-

I. Carbol fuschin

Basic fuschin- 0.5 gm

Absolute alcohol-5 ml

5% aqueous phenol-100 ml

Mix well & filter before use.

II. Methylene blue solution (stock)

Methylene blue-1.4 gm

95% Alcohol -100 ml

III. Working methylene blue solution (working)

Methylene blue -10 ml

Tap water-90 ml

IV.20% sulfuric acid

(1% sulphuric acid for Nocardia, 5% sulphuric acid for Mycobacteriumtuberculosis) Procedure

1. Make a smear and allow it to dry at room temperature.

2. Flood the slide with carbol fuschin and heat gently until the steam isseen rising from the slide. Do not bring to boil.

3. Heat intermittently for 10 mins.

4. Wash well in tap water.

5. Differentiate in acid alcohol (2-5 dips).

6. Flood the slide with 20% sulphuric acid. Leave this until the smear ispale pink in color.

7. Rinse in tap water.

8. Counterstain with methylene blue till smear is pale blue.

9. Rinse in tap water. Grocott's Methamine Silver Stain

Components: Methenamine silver nitrite

Stock solution: Mix 100 ml of 3% methenamine and 5 ml of 5% silvernitrate. Shake well.

Working solution: Mix 25 ml of stock solution with 25ml of distilled water and 2ml of 5% sodium borate. Fast green

Stock solution: dissolve 0.2 gm of fast green in 100 ml 0.2% acetic acid

Working solution: mix 10ml of stock solution with 40 ml of distilled water

4% solution of chromium trioxide

1% solution of sodium bisulfate

0.2% solution of gold chloride

2% solution of sodium thiosulfate

Fixation: 70% ethyl alcohol for 1 minute

50% ethyl alcohol for 1 minute

Staining procedure

1. Give 15 dips in distilled water

2. Pour 5% chromium trioxide for 2 minutes

3. Coplin jar is transferred to 50degree C water bath and kept for 15 minutes

4. Give 15 dips in tap water

5. Pour 1% sodium bisulfate for 30 seconds

6. Wash under running tap water for 15 minutes

7. Give 15 dips in distilled water

8. Give 15 dips in distilled water

9. Give 15 dips in distilled water

10. Give 15 dips in distilled water

11. Pour Methanamine silver solution and keep for 2 minutes (place coplin jar with solution and slides in 43 degree C water bath)

12. Coplin jar is transferred to 58 degree C

13. Give 15 dips in distilled water
14. Give 15 dips in distilled water
15. Give 15 dips in distilled water
16. Give 15 dips in distilled water
17. Give 20 to 30 dips in 0.2% gold chloride
18. Give 15 dips in distilled water
19. Give 15 dips in distilled water
20. Pour 2% sodium thiosulfate for 1 minute
21. Wash under Running tap water for 15 seconds
22. Fast gram for 30 seconds
23. Wash under Running tap water 15 seconds
24. Give 15 dips in distilled water
25. Give 15 dips in distilled water
26. Give 15 dips in 95% ethyl alcohol
27. Give 15 dips in 95% ethyl alcohol
28. Give 15 dips in 95% ethyl alcohol
29. Give 15 dips in absolute ethyl alcohol
30. Give 15 dips in absolute ethyl alcohol
31. Give 15 dips in absolute xylene

PAS Stain (Periodic Acid Schiff Stain)

**Components:**

1% periodic acid

Schiff reagent

- Distilled water 100ml
- Basic fuschin 1gm
- Sodium metasulphite 2gm
- 1N HCL 20ml
- Activated charcoal 0.3mgm

Sodium metasulphite solution

- Stock solution 10% aqueous solution
- Working solution 5% of stock solution + 100 ml distilled water

Oxalic acid 0.5 gm

Potassium sulphite 0.5 gm

Distilled water 100 ml

1% acetic acid 100ml Fixation – 70% ethyl alcohol

50% ethyl alcohol

1% hematoxylin

**Procedure**

1. Give 15 dips in distilled water
2. Pour Periodic acid for 10 minutes
3. Wash under Running tap water for 10 minutes
4. Pour Distilled water for 15 minutes
5. Pour Schiff reagent for 15 minutes
6. Pour Sodium metasulphite 6 minutes
7. Wash under Running tap water for 10 minutes
8. Pour Hematoxylin for 4 minutes
9. Wash under Running tap water for 5 to 10 minutes
10. Wash under Running tap water for 5 minutes
11. Pour Distilled water and keep for 5 minutes
12. Give 15 dips in Distilled water
13. Give 15 dips in 95% ethyl alcohol
14. Give 15 dips in 95% ethyl alcohol
15. Give 15 dips in absolute alcohol
16. Give 15 dips in absolute alcohol
17. Give 15 dips in xylene

Procedure to make cell block

1. A separate pass was given to collect material for making cellblocks.
2. Suck 20 ml of 10% formalin into the syringe immediately.
3. Put the material with formalin into test tube and leave for 6 hours.
4. Centrifuge the material for 5 minutes and wash with phosphate buffered saline (PBS).Repeat it 3 times.
5. Put 100 ml pooled plasma into button and mix it.
6. Add 25-40 ml of thrombin segment.
7. Leave till the clot is formed.
8. Give it for tissue processing.

Immunohistochemistry - standard Strept Avidin Procedure

1. 2-3 mm sections were cut and mounted on Poly L-lysine coated slides.

Slides were dried overnight at 37°C and dewaxed in xylene and hydrated.

2. Sections were put on Poly L-lysine coated slides and incubated at 60°C for 30 min. The temperature was adjusted at 37°C after 30 minutes. The slides were left in incubator for overnight.

3. All slides were dewaxed by heating with spirit lamp.

Xylene 3 changes for 10 minutes

| | |
|---|---|
| xylene/ alcohol | 1 change for 10 minutes |
| 100% alcohol | 1 change for 5 minutes |
| 95% alcohol | 1 change for 5 minutes |
| 80% alcohol | 1 change for 5 minutes |
| 70% alcohol | 1 change for 5 minutes |

Finally all slides were rinsed in running tap water.

4. Antigen retrieval procedure - The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it.

5. The black box was placed in microwave for 9 min.

6. Boiling of the solution was observed and the microwave was reset for 6 min and started.

7. The box was removed and cooled in running tap water.

8. Blocking endogenous peroxidase-sections were incubated at roomtemperature in 0.3% H2O2 in methanol for 30 to 45 minutes and rinsed inrunning tap water for 5 to 10 minutes, and dipped in distilled water for 1 minute.

9. The slides were placed in Tris buffer (only 1 change for 5 min).

10. Blocking reagent was applied for 5 - 10 min. The excess blocking reagent was wiped off.

11. Primary antibodies were applied covering the whole tissue and incubated at room temperature for 1 hours.

12. Slides were then washed in Tris buffer for 5 minutes (4 changes).

13. The slides were cleaned with tissue paper.

14. Ultra Vision One HRP Polymer covering the whole tissue was applied and incubated at room temperature for 45 minutes.

15. Washing was done in TBS buffer (Tris buffered saline) for 5 minutes (4changes).

16. One drop of substrate- DAB (3,3-Diaminobenzidine) solution wasapplied on each slide covering the whole material.

17. lncubated for 10-1 5 min.

18. All slides were washed in deiodinized water.

19. Hematoxylin was applied for few seconds.

20. The slides were put in running tap water.

21. They were allowed to dry and dehydrate in alcohol.

22. Incubated for 2 min and allowed to dry.

23. Mounted in DPX (distyrene dibutyl phthalate xylene).

24. The slides were examined microscopically.

**STATISTICAL ANALYSIS**

Data were described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

# OBSERVATIONS AND RESULTS

A total of 9088 cases of fine needle aspiration cytology were received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 5 years from 1st July 2016 - 30th June 2021 (3.5 years retrospectively and 1.5 years prospectively). Out of these102 cases were FNAC from mediastinal lesions.

**Age distribution of patients**

The commonest age group who underwent fine needle aspiration cytology of mediastinal lesions was 51-60 years [n=28, 27.45%] followed by age group of 21 to 30 years [n=19, 18.63%]. The youngest patient was 2 years old while the oldest patient was 81 years old .Mean age was 46.63 years.

**Table 1-Age distribution [n=102]**

| Age group(years) | No.of cases | Percentage |
|---|---|---|
| 0-10 | 1 | 0.98% |
| 11 to 20 | 4 | 3.92% |
| 21 to 30 | 19 | 18.63% |
| 31-40 | 17 | 16.67% |
| 41-50 | 11 | 10.78% |
| 51-60 | 28 | 27.45% |
| 61-70 | 15 | 14.71% |
| >70 | 7 | 6.86% |
| Mean | 46.63 | |
| Range | 2-81 | |

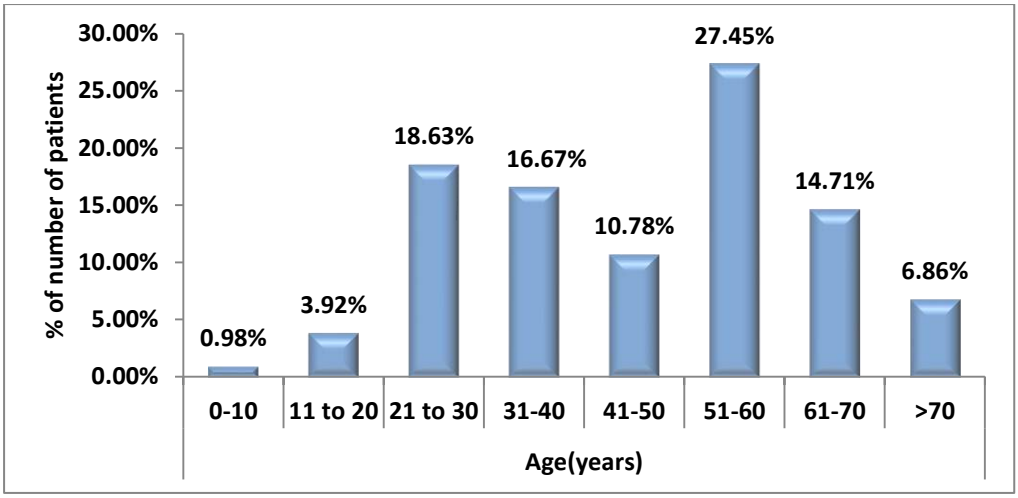


**Figure 1- Age distribution (years)**

### Gender Distribution of patients

Overall incidence of mediastinal lesions was higher in males constituting 59.80% (n=61) of the patients. The male to female ratio was 1.4:1

**Table 2- Gender distribution [n=102]**

| Sex | No. of Cases | Percentage |
|---|---|---|
| Males | 61 | 59.80% |
| Females | 41 | 40.20% |

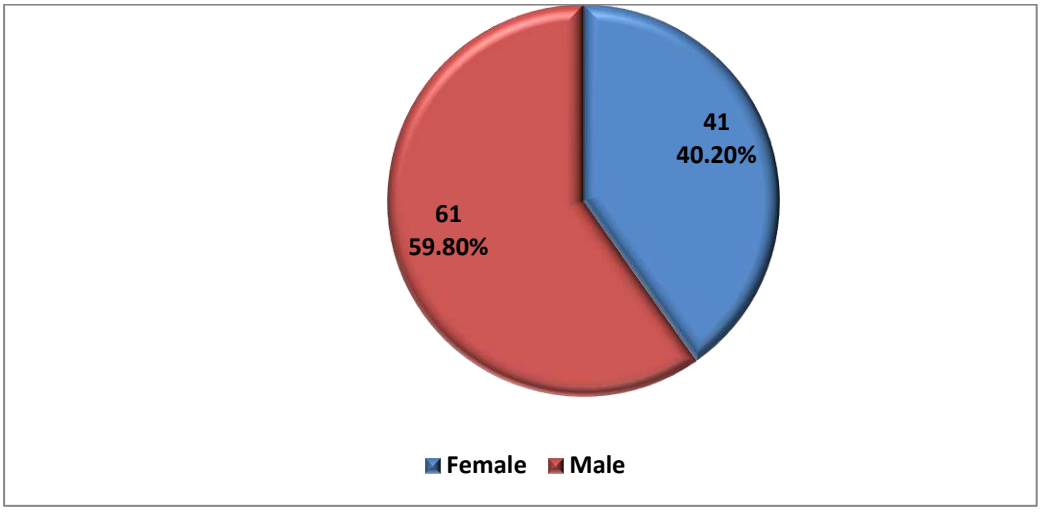


**Figure 2- Gender distribution (n=102)**

**Clinical presentation of patients**

Majority of patients presented with fever and cough [n=44, 43.14%] followed by loss of weight [n=31, 30.39%]. Some patients presented with more than one symptom, so there was overlap in categorizing patients on the basis of clinical symptoms.

**Table 3 -Clinical presentation [n=102]**

| Presenting Symptoms | No. of Cases | Percentage |
|---|---|---|
| Fever | 44 | 43.14% |
| Cough | 44 | 43.14% |
| Loss of weight | 31 | 30.39% |
| Dyspnea | 24 | 23.53% |
| Loss of appetite | 22 | 21.56% |
| Chest pain | 17 | 16.67% |

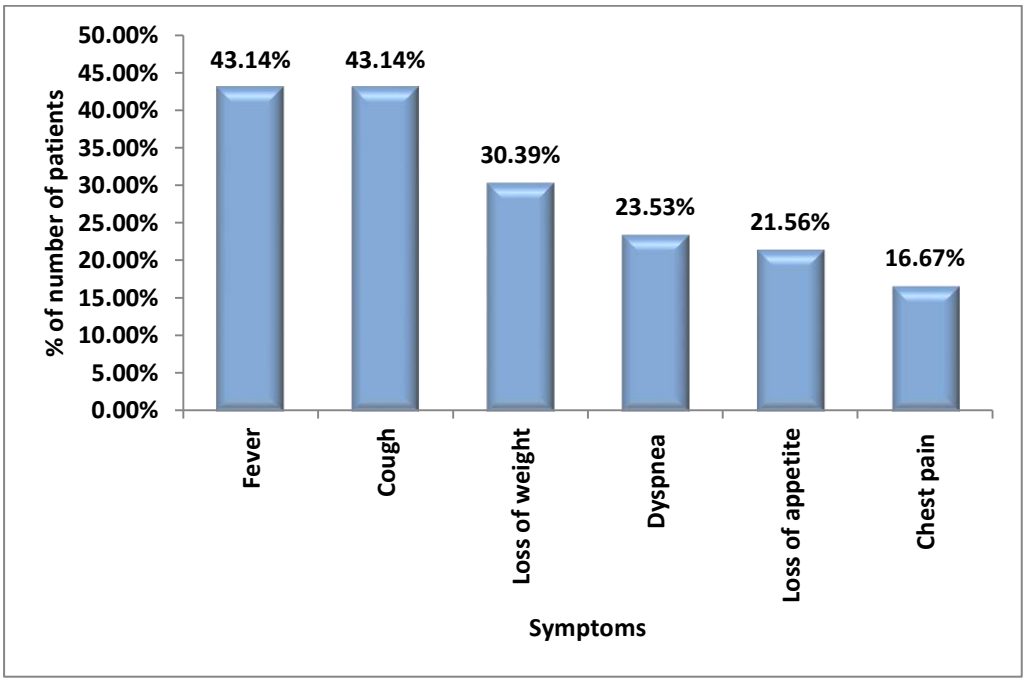


**Figure 3- Clinical presentation (n=102)**

**Site of mediastinal lesions**

Majority of patients presented with lesions in the anterior/superior mediastinum [n=60, 58.82%] followed by middle mediastinum [n=33, 32.35%]. Posterior mediastinum was involved in only 7 out of 102 patients [6.86%]. Multiple compartments were involved in 2 cases (1.96%)

**Table 4 - Site of mediastinal lesions [n=102]**

| Site | No. of Cases | Percentage |
|---|---|---|
| Anterior / superior Mediastinum | 60 | 58.82% |
| Middle Mediastinum | 33 | 32.35% |
| Posterior Mediastinum | 07 | 6.86% |
| Multiple compartments | 02 | 1.96% |

**Mode of FNAC**

Majority of patients underwent ultrasound guided FNAC [n=54, 52.94%] followed by Endoscopic USG guided [n=35, 34.31%] and CT guided [n=13, 12.75%].

**Table 5-Mode of Fine needle aspiration cytology [n=102]**

| Mode of FNAC | No. of cases | Percentage |
|---|---|---|
| Ultrasound guided | 54 | 52.94% |
| Endoscopic ultrasound guided | 35 | 34.31% |
| Computed tomography guided | 13 | 12.75% |

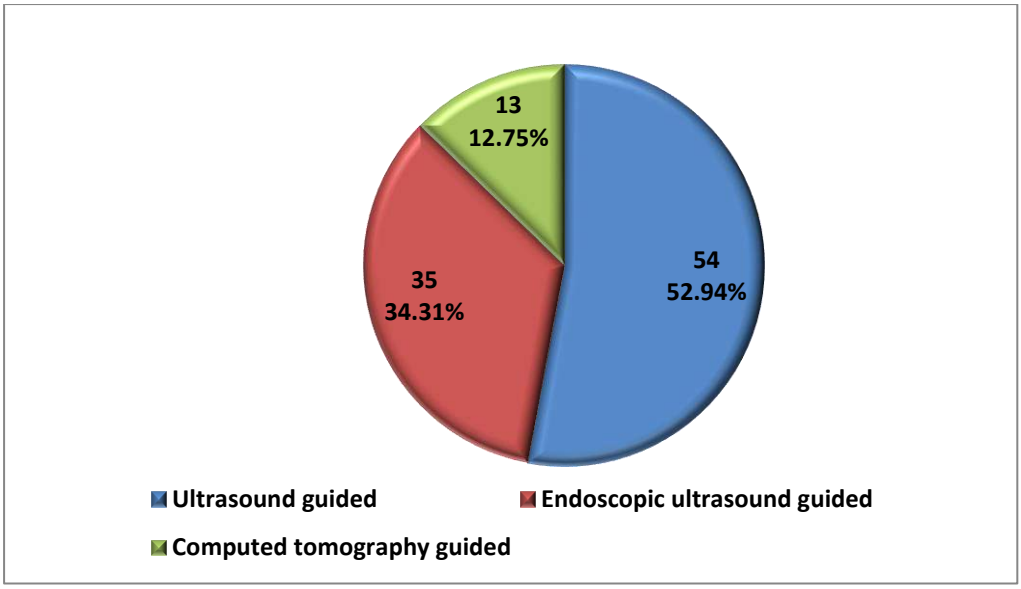


**Figure 4- Mode of FNAC (n=102)**

**Spectrum of radiological lesions**

Among the radiological findings in the patients, the commonest was mediastinal mass which was seen in 54.90% followed by mediastinal lymphadenopathy [LAP] in 45.10%

**Table 6: Spectrum of Radiological lesion (n=102)**

| Radiological lesion | No. of patients | Percentage |
|---|---|---|
| Mediastinal Mass | 56 | 54.90% |
| Mediastinal LAP | 46 | 45.10% |

**Cytological categorisation of mediastinal lesions**

All the cases were categorized into three broad categories as Non diagnostic, Non-neoplastic and Neoplastic for evaluation.

Non diagnostic-This category included cases with insufficient quantitative and/or qualitative cellular material to make a definite cytological diagnosis.

Non neoplastic-This included specimens lacking evidence of neoplastic process. It comprised of inflammatory, metaplastic, infective and reactive lesions which includes acute, chronic and granulomatous

inflammation like tuberculosis, sarcoidosis, cysts like thymic cyst, bronchogenic cysts, reactive hyperplasia of lymph node and acute suupurative pathology.

Neoplastic**–**The aspirates which were diagnostic of malignancy such as Hodgkin's lymphoma, Non-Hodgkin's lymphoma, germ cell tumors, carcinoid tumor, neuroendocrine carcinoma, sarcomas and metastasis were part of this category.

**Table 7 -Cytological categorization of mediastinal lesions[n=102]**

| Category | No. of Cases | Percentage |
|---|---|---|
| Non diagnostic | 28 | 27.45% |
| Non-neoplastic | 35 | 34.31% |
| Neoplastic | 39 | 38.24% |

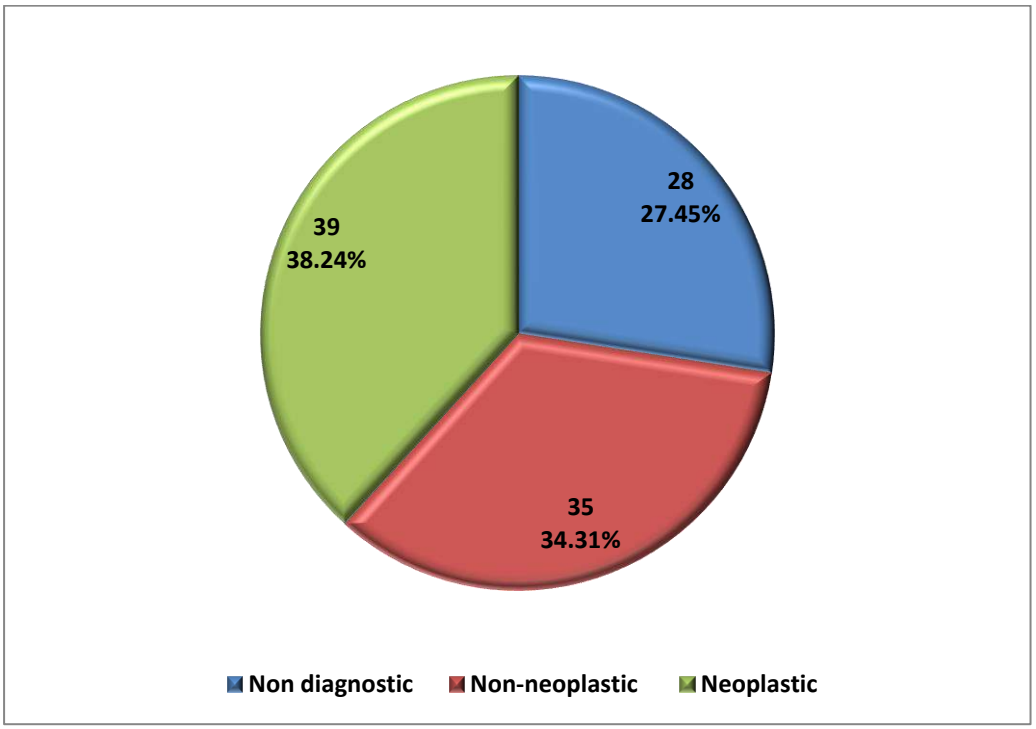


**Figure 5- Cytological categorization of mediastinal lesions (n=102)**

The majority of the cases were grouped under Neoplastic category which comprised of 38.24% [n=39] of all the cases followed by Non-Neoplastic [35, 34.31%]. 28 out of 102 patients [27.45%] were categorized as non-diagnostic.

Histopathological correlation was done in 36 cases out of 102 either with surgical biopsy or cell block.

**NON- DIAGNOSTIC FOR EVALUATION (n=28)**

**Age distribution of Non-Diagnostic Category**

The most common age group was found to be 51-60 years [n=8, 28.57%] followed by 31-40 years [n=6, 21.42%] with a mean age of 46.30 years

**Table 8 – Age distribution of Non-diagnostic lesions [n=28]**

| Age group (years) | No. of cases | Percentage |
|---|---|---|
| 0-10 | 0 | 00 |
| 11-20 | 2 | 7.14% |
| 21-30 | 5 | 17.85% |
| 31-40 | 6 | 21.42% |
| 41-50 | 1 | 3.57% |
| 51-60 | 8 | 28.57% |
| 61-70 | 4 | 14.28% |
| >70 | 2 | 7.14% |
| Mean age | 46.30 | |
| Range | 12-79 | |

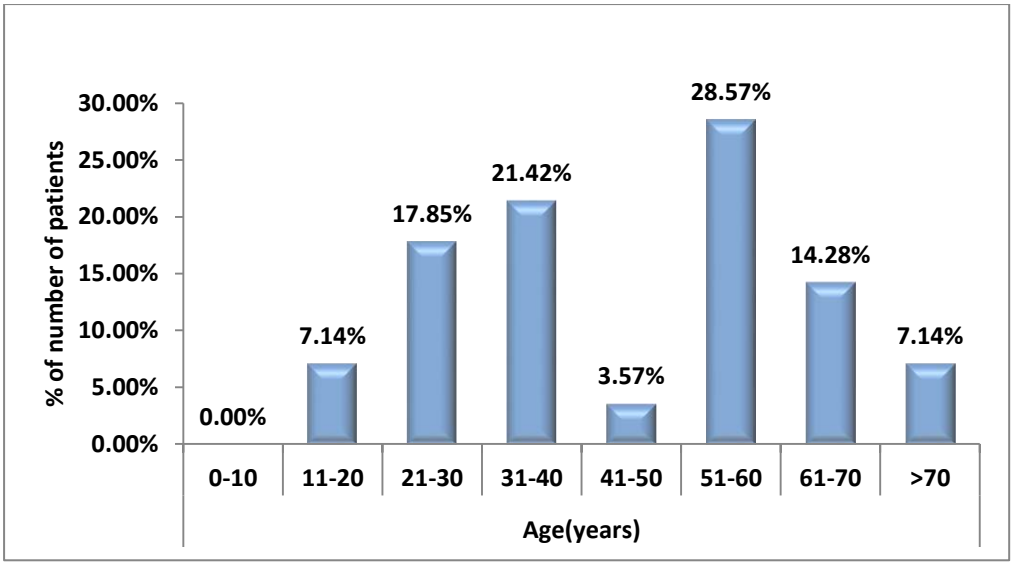


**Figure 6- Age distribution (years) of non-diagnostic lesions (n=28)**

**Gender distribution of Non-diagnostic lesions**

Slight male predominance was noted with 15 [53.57%] cases being males and13 [46.43%] females. The male to female ratio was 1.1:1

**Table 9 - Gender distribution of Non-Diagnostic lesions [n=28]**

| Sex | No. of cases | Percentage |
|---|---|---|
| Males | 15 | 53.57% |
| Females | 13 | 46.43% |

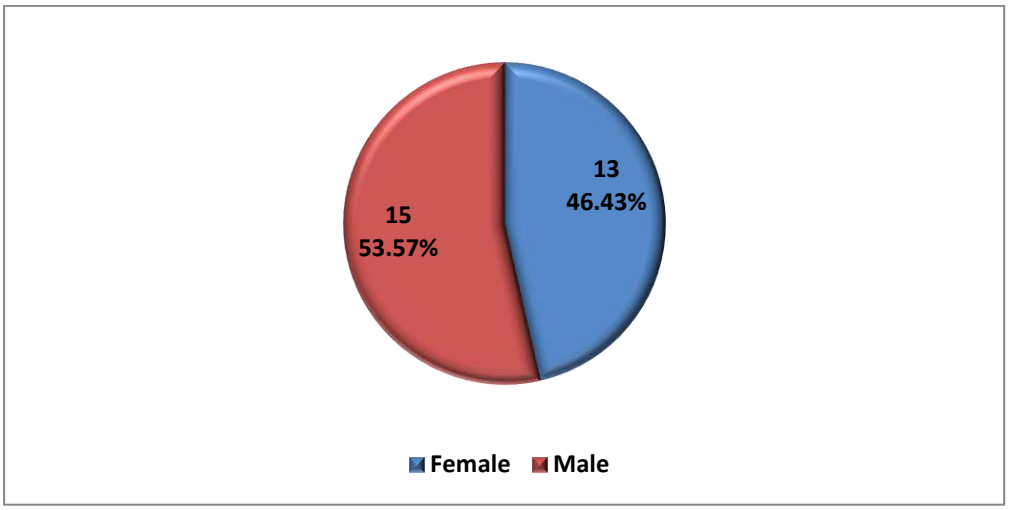


**Figure 7- Gender distribution of non-diagnostic lesions (n=28)**

**Mode of FNAC in Non-diagnostic Category**

In majority of the patients in Non- diagnostic category, mode of FNAC was EUS guided [n=13, 46.43%] followed by USG guided [n=10, 35.71%] and CT guided [n=5, 17.86%] FNACs. EUS FNAC done under real time ultrasound using a through-the-scope needle aspiration was associated with inadequate yield more frequently when compared with USG guided FNAC.

**Table 10 -Mode of FNAC in Non-Diagnostic Category [n=28]**

| Mode of FNAC | No. of cases | Percentage |
|---|---|---|
| EUS guided | 13 | 46.43% |
| USG guided | 10 | 35.71% |
| CT guided | 5 | 17.86% |

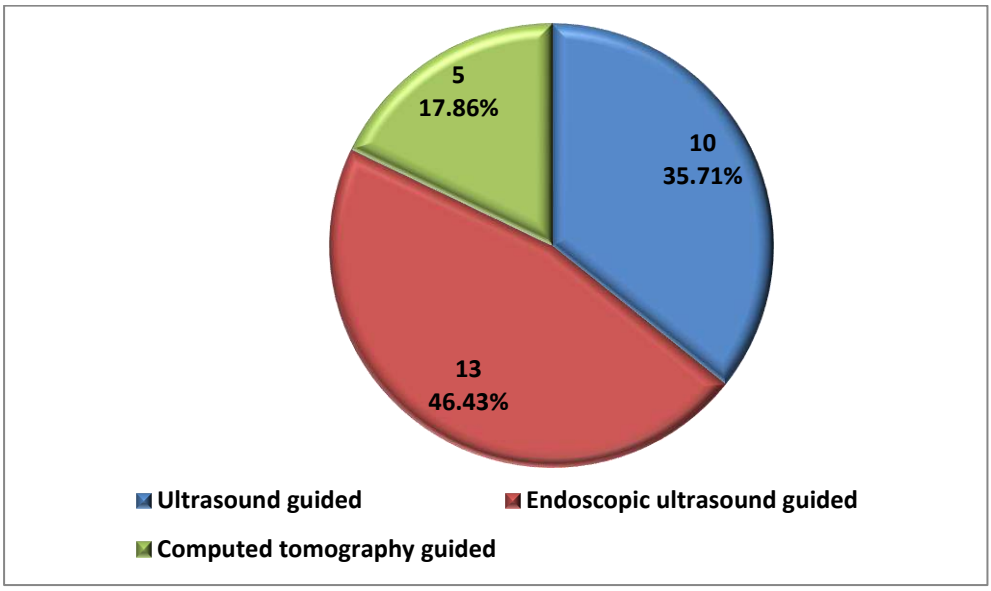


**Figure 8- Mode of FNAC of non-diagnostic lesions (n=28)**

**Site of mediastinal lesions**

Majority of patients presented with lesions in the anterior mediastinum [n=10, 35.71%] followed by middle mediastinum [n=09, 32.14%] and superior mediastinum [n=04, 14.28%]. Posterior mediastinum was

involved in only 03 out of 28 patients [10.71%]. Two patients (7.14%) had masses involving multiple compartments of the mediastinum.

**Table 11: Site of mediastinal lesions in Non - diagnostic Category [n=28]**

| Site | No. of cases | Percentage |
|---|---|---|
| Anterior mediastinum | 10 | 35.71% |
| Middle mediastinum | 09 | 32.14% |
| Superior mediastinum | 04 | 14.28% |
| Posterior mediastinum | 03 | 10.71% |
| Multiple compartments | 02 | 7.14% |

**Table 12- Causes for Non diagnostic Category [n=28]**

| Reason for Non diagnosis | No. of Cases | Percentage |
|---|---|---|
| Scantily cellular | 18 | 64.29% |
| Hemorrhagic smear | 8 | 28.57% |
| No cellularity | 02 | 7.14% |

Out of the 28 cases which were grouped under this category 02 cases had no diagnostic material, 18 had scanty cellularity and 08 were unsatisfactory due to blood obscuring the cells, hence a final diagnosis could not be reached in any of them. All these cases were classified as non diagnostic for evaluation.

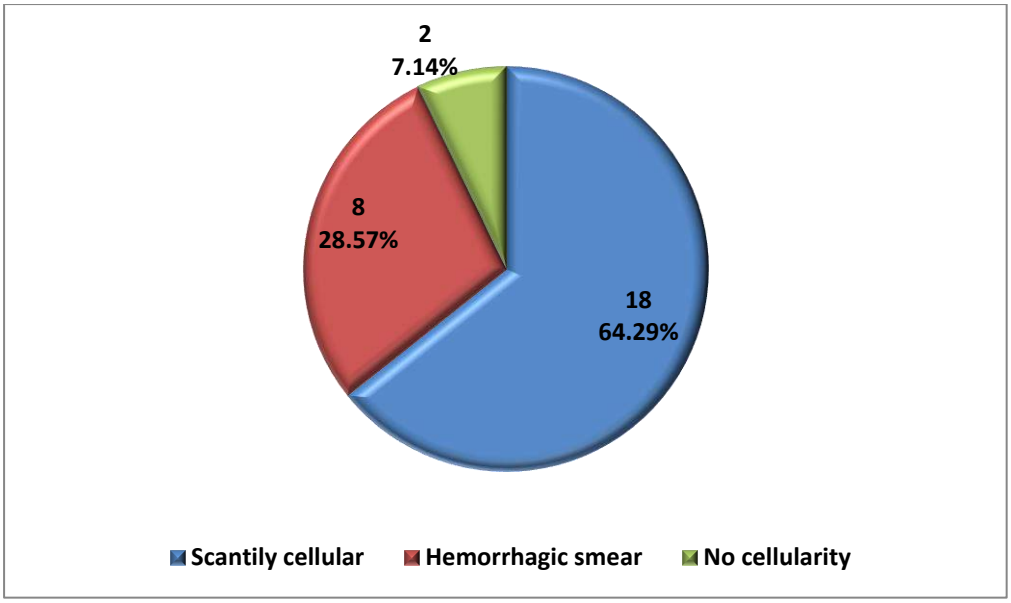


**Figure 9- Causes for non-diagnostic category**

Out of the 28 cases in non-diagnostic category, histopathology was available in only 04 cases. These cases were diagnosed each as Fungal granulomas having aspergillus, Neurogenic tumor, Granulomatous inflammation-TB and Metastatic adenocarcinomatous deposits from GIT origin on histology and IHC respectively.

**Table 13- Cytological-histological correlation for Non diagnostic Category- [n=04]**

| Histopathological diagnosis | No. of cases |
|---|---|
| Fungal granulomas(Aspergillus) | 01 |
| Granulomatous inflammation-TB | 01 |
| Neurogenic tumor with low proliferative index | 01 |
| Metastatic Adenocarcinomatous deposits from GIT | 01 |

**NON-NEOPLASTIC CATEGORY (n=35)**

**Age distribution of Non-Neoplastic Category**

In the Non-neoplastic category, the most common age group was found to be 21-30 years [n=9, 25.71%] 51-60 years [n=8, 22.85%] with

a mean age of 19.30 years .The youngest patient was 16 years old while the oldest patient was 76 years old.

**Table 14- Age distribution of Non-neoplastic Category [n=35]**

| Age group [Years] | No. of Cases | Percentage |
|---|---|---|
| 0-10 | 0 | 00 |
| 11-20 | 1 | 2.85% |
| 21-30 | 9 | 25.71% |
| 31-40 | 8 | 22.85% |
| 41-50 | 5 | 14.28% |
| 51-60 | 8 | 22.85% |
| 61-70 | 2 | 5.71% |
| >70 | 2 | 5.71% |
| Mean age | 19.30 | |
| Range | 16-76 | |

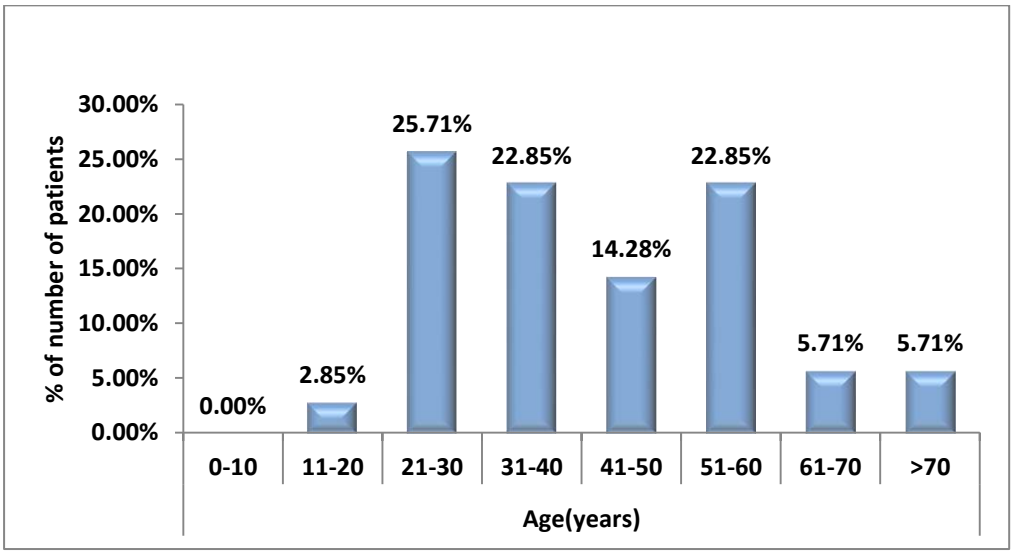


**Figure 10-Age distribution (years) of Non-neoplastic lesions (n=35)**

**Gender distribution of Non-neoplastic Category**

19 [54.29%] were males forming the majority whereas 16 [45.71%] of the patients were females .The male to female ratio was 1.2:1

**Table 15-Gender distribution of Non-neoplastic lesions (n=35)**

| Sex | No. of cases | Percentage |
|---|---|---|
| Males | 19 | 54.29% |
| Females | 16 | 45.71% |

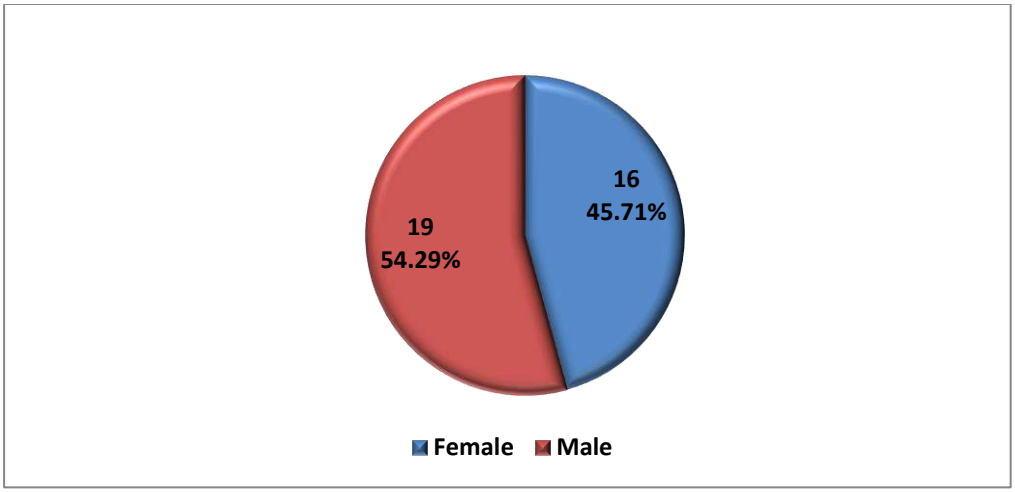


**Figure 11-Gender distribution of Non-neoplastic lesions (n=35)**

**Clinical presentation of patients in Non-neoplastic Category**

Most common clinical presentation of patients in the Non-neoplastic category was fever [n=16, 47.05%] followed by cough [n=12, 35.29%]. Here too some patients presented with more than one symptom.

**Table 16 – Clinical presentation of patients with Non-neoplastic lesions (n=35)**

| Presenting symptom | No. of cases | Percentage |
|---|---|---|
| Fever | 16 | 47.05% |
| Cough | 12 | 35.29% |
| Dyspnea | 6 | 17.64% |
| Chest pain | 4 | 11.76% |
| Loss of weight | 6 | 17.64% |
| Loss of appetite | 3 | 8.82% |

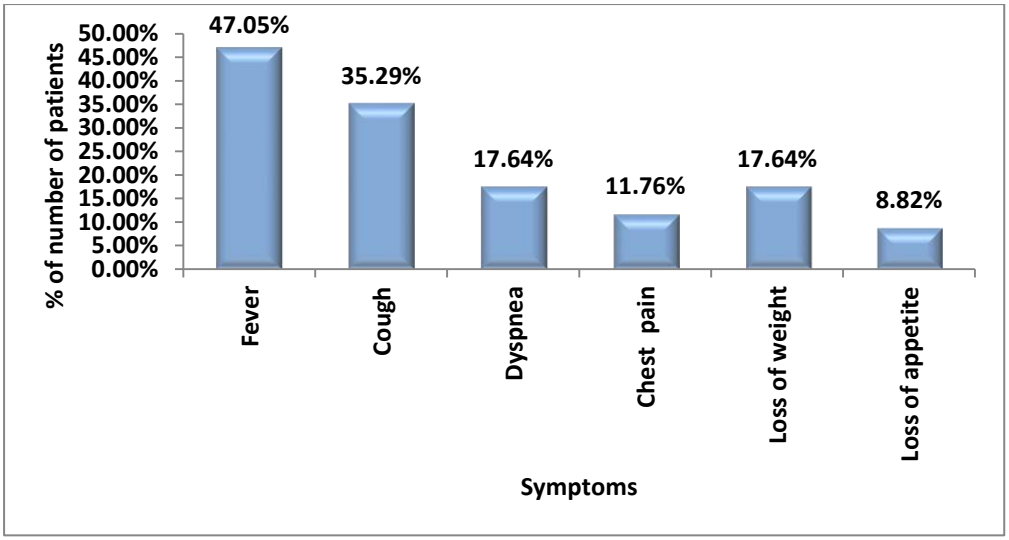


**Figure 12- Clinical presentation of patients with non-neoplastic lesions**

### Mode of FNAC of Non-neoplastic Category

In majority of the patients mode of FNAC was EUS guided [n=22, 62.86%] followed by USG guided [n=10, 28.57%]

**Table 17 -Mode of FNAC of Non-neoplastic Category [n=35]**

| Mode of FNAC | No. of cases | Percentage |
|---|---|---|
| EUS guided | 22 | 62.86% |
| USG guided | 10 | 28.57% |
| CT guided | 3 | 8.57% |

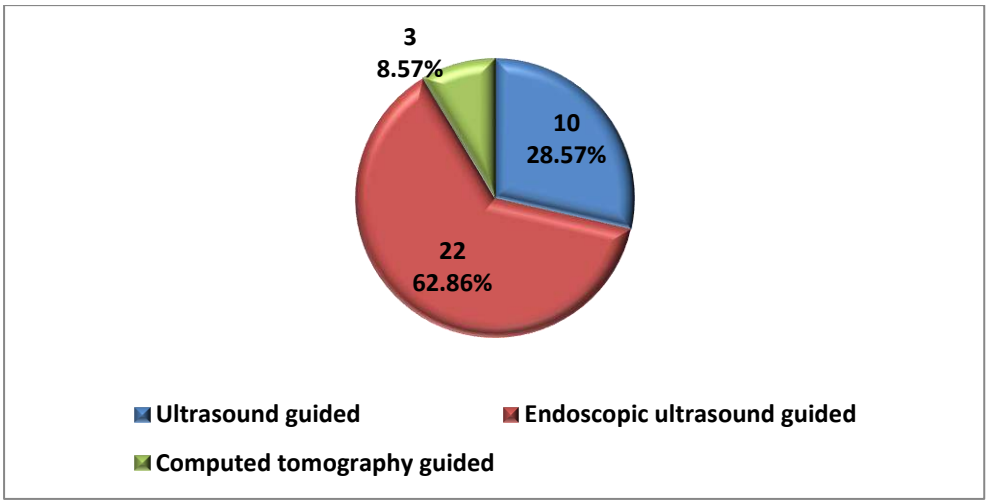


**Figure 13- Mode of FNAC of Non-neoplastic lesions (n=35)**

**Diagnostic Spectrum of lesions in Non-neoplastic Category**

Granulomatous inflammation/lymphadenitis [n=27, 77.14%] was the most frequently made diagnosis followed by reactive hyperplasia [n=3,8.57%] of lymph node. Acute suppurative pathology was diagnosed in 2 cases and non specific inflammation was diagnosed in only 1 out of 35 patients.

**Table 18- Cytological diagnostic spectrum of Non-neoplastic lesions [n=35]**

| **Cytological diagnosis** | **Radiological findings** | **Anterior mediastinum** | **Middle mediastinum** | **Superior mediastinum** | **Posterior mediastinum** | **Percentage** |
|---|---|---|---|---|---|---|
| Granulomatous inflammation (n=27) | Mediastinal LAP-25 Mediastinal mass-02 | 10 | 13 | 04 | - | 77.14 % |
| Reactive hyperplasia Lymph node (n=03) | Mediastinal LAP-03 | 02 | 01 | - | - | 8.57% |
| Benign cystic lesion (n=02) | Mediastinal mass-02 | 02 | - | - | - | 5.71% |
| Non specific inflammation (n=01) | Mediastinal LAP- 01 | | 01 | - | - | 2.85% |
| Acute suppurative pathology(n=02) | Mediastinal LAP-01<br>Mediastinal abcess-01 | - | - | 01 | 01 | 5.71% |

Granulomatous inflammation was seen as collections of epithelioid cells forming granulomas with or without necrosis/inflammatory cells or giant cells. In one case, additional features like Schaumann bodies and Asteroid bodies were also seen, hence diagnosis of Sarcoidosis was made. Reactive hyperplasia of lymph node was seen as lymphoid cells in varying stages of maturation seen as centrocytes, centroblasts, immunoblasts, plasma cells and tingible body macrophages diagnosed in 3 cases accounting for 8.82% of the total cases. 2 cases were cystic lesions of anterior mediastinum in which smears had sheets of foamy macrophages along with few epithelial cells. Non specific inflammation of middle mediastinal lymph node was seen in one [2.85%] case which had many inflammatory cells like neutrophils and lymphocytes. Special stains like 20% ZN stain for AFB, PAS and GMS stains for fungus were negative in this case. Acute suppurative pathology was seen in 2 cases [5.71%]. Pus was aspirated and the smears had sheets of degenerated and viable neutrophils. Necrosis and giant cells were also seen. However noepithelioid cell granuloma/fungal profile were seen. Special stains were also negative in these cases.

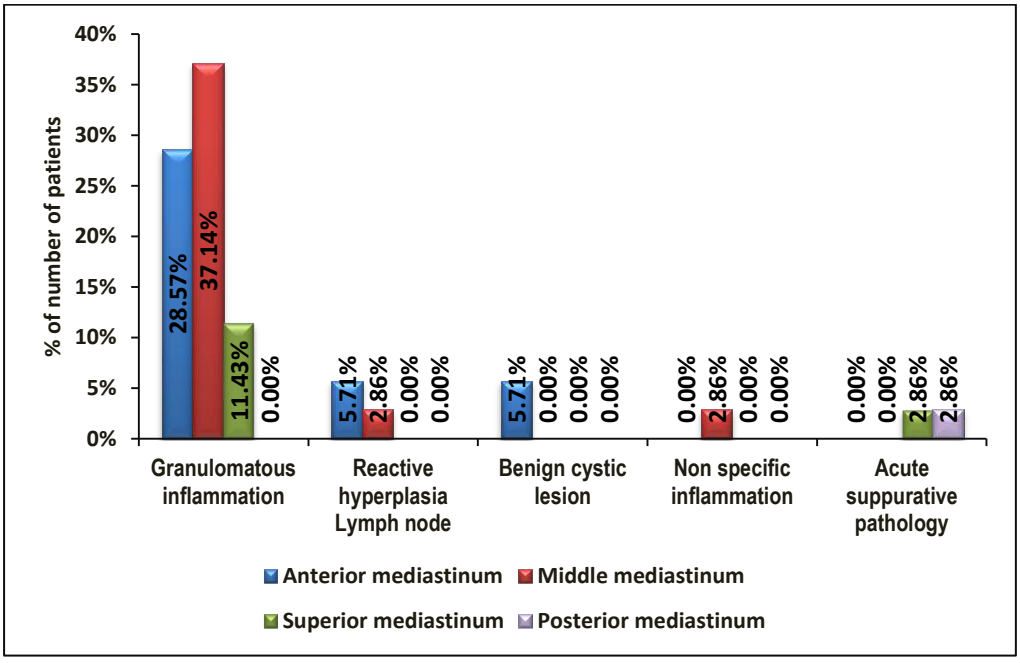


**Figure 14- Cytological diagnostic spectrum of Non-neoplastic lesions (n=35)**

**Table 19- Correlation of 20% ZN status on fine needle aspiration (FNA) material, clinical outcome and microbiological results of cases of Granulomatous inflammation (n=27)**

| Granulomatous inflammation | Positive No. of cases | Percentage | Negative No. of cases | Percentage |
|---|---|---|---|---|
| ZN Stain (FNAC) | 6 | 22.22% | 21 | 77.77% |
| K/C/O tuberculosis | 8 | 29.62% | 19 | 70.37% |
| Culture for mycobacterium Tuberculosis | 02 | 7.40% | 06 | 22.22% |

In the non-neoplastic category, granulomatous inflammation was the most frequently diagnosed lesion (n=27, 77.14%) of which 6 cases [22.22%] were positive for acid fast bacilli [AFB] on 20% Ziehl-Neelsen [ZN] stain and 21 [77.77%] cases were AFB negative. AFB was highlighted on 20% Ziehl-Neelsen stain as slender beaded rods of bacilli 1-4um in length. 8 cases were known case of pulmonary TB and were on ATT for the same. Mycobacterial infection was diagnosed in 8 cases, two by positive culture for M. tuberculosis and six by positive staining for AFB .In addition, 8 cases were known case of TB. Thus a final diagnosis of TB was made in 16 cases (15.68%) of all the cases.

**Cyto-histopathological correlation in Non-Neoplastic Category**

Cytological-histological correlation was done in those cases in which biopsywas received or cell block had adequate material. Out of the 35 cases in non-neoplastic category, only 04 cases had availability of histopathology material. All the 4 cases were concordant with cytological diagnosis.

**Table 20- Cyto-histopathological correlation of Non-neoplastic lesions (n=04)**

| Cytological diagnosis | Histopathological diagnosis | Cases |
|---|---|---|
| I. Granulomatous inflammation-TB [n=02] | Granulomatous inflammation-TB<br>Tuberculosis with candidiasis | 01<br>01 |
| II. Granulomatous inflammation-Sarcoidosis [n=01] | Sarcoidosis | 01 |
| III. Non specific Inflammation [n=01] | Inflammatory pathology acute and chronic, non specific | 01 |

No cyto-histological discordance was evident in any of the 4 cases.

**NEOPLASTIC CATEGORY (n=39)**

**Age distribution in Neoplastic Category**

Majority of the cases belonged to the age group of 51-60 years [10, 25.64%] followed by 61-70 years [8, 20.51%] with mean age of 59.80 years.

**Table 21- Age distribution of Neoplastic lesions [n=39]**

| Age group(Years) | No. of Cases | Percentage |
|---|---|---|
| 0-10 | 1 | 2.56% |
| 11-20 | 2 | 5.12% |
| 21-30 | 5 | 12.82% |
| 31-40 | 4 | 10.25% |
| 41-50 | 5 | 12.82% |
| 51-60 | 10 | 25.64% |
| 61-70 | 8 | 20.51% |
| >70 | 4 | 10.25% |
| Total | 39 | 100.00% |
| Mean age | 59.80 | |
| Range | 2-81 | |

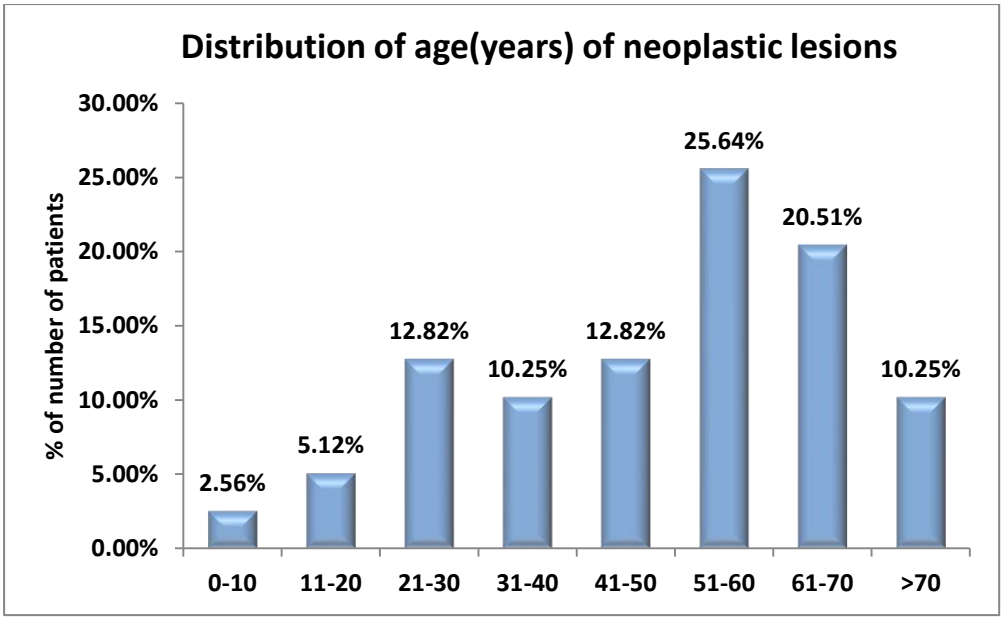


**Figure 15-Age distribution (years) of neoplastic lesions (n=39)**

### Gender distribution in Neoplastic Category

Out of 39 neoplastic cases, 29 [74.36%] were males whereas 10 [25.64%] were females. The male to female ratio was 2.9:1

**Table 22 - Gender distribution of Neoplastic lesions [n=39]**

| Gender | No. of Cases | Percentage |
|---|---|---|
| Male | 29 | 74.36% |
| Female | 10 | 25.64% |

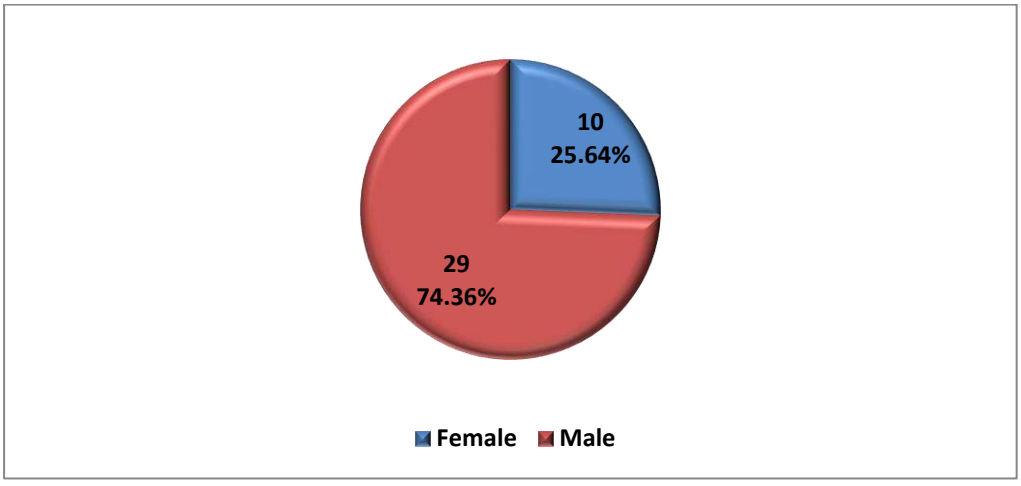


**Figure 16- Gender distribution of neoplastic lesions (n=39)**

**Clinical presentation of patients in Neoplastic Category**

Most common clinical presentation of patients in the neoplastic category was cough [20, 51.28%] followed by loss of weight [19, 48.71%]. Some patients presented with more than one symptom.

**Table 23 – Clinical presentation of patients with Neoplastic lesions (n=39)**

| Presenting symptom | No. of cases | Percentage |
|---|---|---|
| Fever | 15 | 38.46% |
| Cough | 20 | 51.28% |
| Dyspnea | 18 | 46.15% |
| Chest pain | 13 | 33.33% |
| Loss of weight | 19 | 48.71% |
| Loss of appetite | 15 | 38.46% |

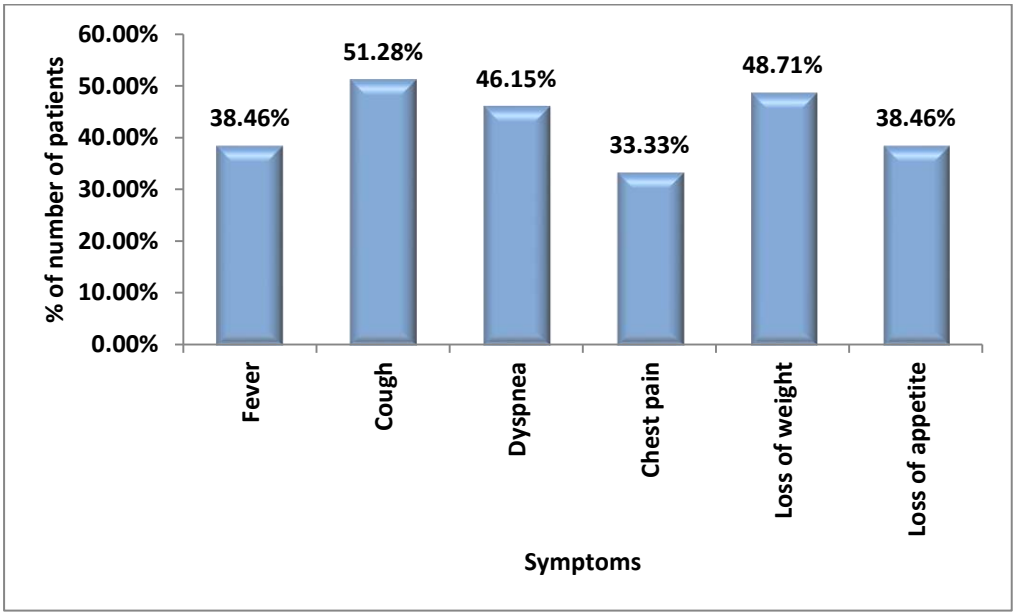


**Figure 17- Clinical presentation of patients with neoplastic lesions**

**Mode of FNAC in Neoplastic Category**

In most of the patients under Neoplastic category, mode of FNAC was ultrasound guided [n=31, 79.49%] followed by CT guided [n=6, 15.38%].

**Table 24 -Mode of FNAC in Neoplastic lesions (n=39)**

| Mode of FNAC | e | Percentage |
|---|---|---|
| USG guided | 31 | 79.49% |
| CT guided | 6 | 15.38% |
| EUS guided | 2 | 5.13% |

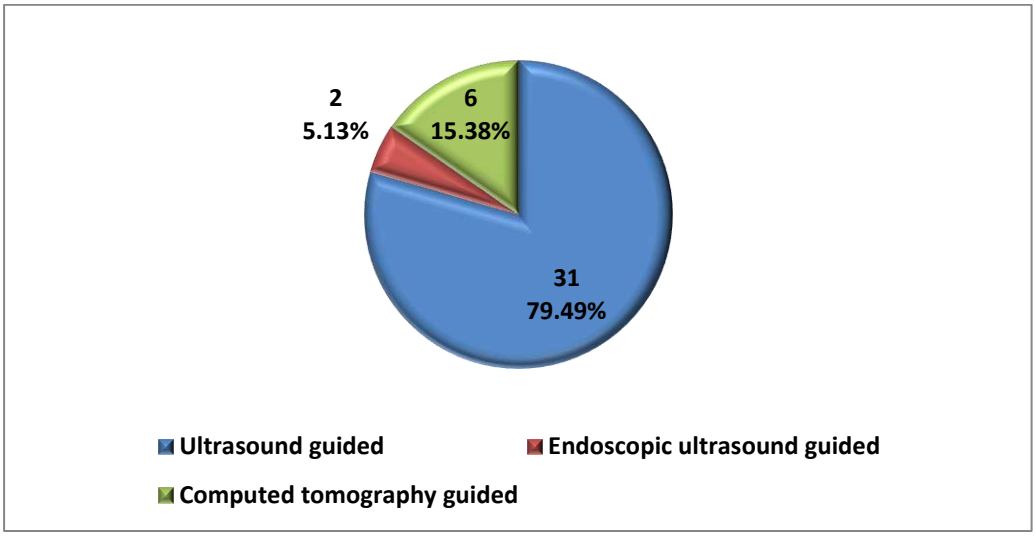


**Figure 18-Mode of FNAC in neoplastic Category (n=39)**

**Table 25- Diagnostic spectrum of Neoplastic Category [n=39]**

| Cytological diagnosis | Radiological findings | Anterior mediastinum | Midde mediastinum | Superior mediastinum | Posterior mediastinum | Percentage |
|---|---|---|---|---|---|---|
| Lymphoma (n=12) | Mediastinal mass-12 | 09 | 01 | 01 | 01 | 30.76% |
| Metastatic Tumor (n=09) | Mediastinal mass-06 | 05 | 03 | - | 01 | 23.07% |
| | Mediastinal LN-03 | | | | | |
| Carcinoma NOS (n=05) | Mediastinal mass-05 | 02 | 01 | - | 02 | 12.82% |
| Thymoma (n=04) | Mediastinal mass-04 | 02 | 01 | 01 | - | 10.25% |
| Malignant round cell | Mediastinal mass-03 | 02 | 02 | - | - | 10.25% |

| | | | | | | |
|---|---|---|---|---|---|---|
| Tumor (n=04) | Mediastinal Lymph node-01 | | | | | |
| Germ cell tumor (n=02) | Mediastinal mass-02 | 02 | - | - | - | 5.12% |
| Thymic carcinoma (n=01) | Mediastinal mass-01 | 01 | - | - | - | 2.56% |
| Small cell carcinoma (n=01) | Mediastinal mass-01 | | 01 | | | 2.56% |
| Neuroblastic tumor (n=01) | Mediastinal mass-01 | | | | 01 | 2.56% |

In the neoplastic category, Lymphoma [12, 30.76%] was the most common diagnosis on cytology where atypical lymphoid cells were seen in smears. A cytological possibility of Non-Hodgkin lymphoma was rendered in cases where patternless sheets of singly dissociated atypical cells having round nucleus, irregular nuclear contours, inconspicuous nucleoli, fine nuclear chromatin and moderate cytoplasm was seen. A possibility of Hodgkin's lymphoma was made in cases where aspiration smears showed Reed–Sternberg cells/ Hodgkin cells in the background of reactive lymphocytes, plasma cells, eosinophils, and histiocytes. The neoplastic Hodgkin/ReedSternberg (HRS) cells comprised only a minority of the total cell population and were large, atypical mononuclear or binucleated cells with prominent central eosinophilic macronucleoli, perinucleolar clearing and abundant amphophilic cytoplasm. Definite categorization of lymphoma type was made only after IHC evaluation.

There were 4 cases of thymoma diagnosed on cytology. Cytologically, these were seen as loosely cohesive clusters and singly dispersed spindle to oval cells exhibiting mild nuclear pleomorphism, fine nuclear chromatin, inconspicuous nucleoli and moderate cytoplasm admixed with lymphocytes.

Metastatic tumor were seen in 9 cases [26.47%] with known primary malignancy in 7 cases (lung, esophagus and pleura) and 2 cases were of unknown primary sites. The cytological diagnosis of cases with known primary matched with the morphology of the primary malignancy. Metastatic Neuroendocrine tumor was cytologically diagnosed in 5 cases which showed monomorphic population of cells having stippled chromatin, inconspicuous nucleoli and scant amount of cytoplasm. Metastatic Squamous cell carcinoma was cytologically diagnosed in 4 cases which showed cells having polygonal shape with variable hyperchromasia, eosinophilic refractile cytoplasm. Fibre cells, tadpole cells and individual cell keratinisation was also noted in these cases.

Four cases of malignant round cell tumor were diagnosed on cytology which showed round nucleus, inconspicuous nucleoli and scant cytoplasm.

Small cell carcinoma was diagnosed cytologically in one case. The smears showed dispersed cell population composed of small to medium sized cells with irregular nuclei, finely granular chromatin with scant cytoplasm. Nuclear moulding and streaking was seen. On histology diagnosis of neuroendocrine tumor was given but further IHC was not available.

One case of neuroblastic tumor was diagnosed in a mass in posterior mediastinum on USG guided FNAC .The smears showed singly dispersed large cells with high N/C ratio, prominent nucleoli and abundant eosinophilic granular cytoplasm – Ganglion cells. Also seen were few clusters of cells with round nuclei, inconspicuous nucleoli and scant cytoplasm- neuroblasts.

Two cases of Germ cell tumors were diagnosed on cytology, one case was of seminoma and the other was non-seminomatous germ cell tumor. Cytology of seminoma showed dispersed as well as loose clusters of large cells having rounded nuclei, prominent single or multiple nucleoli and abundant fragile cytoplasm against a tigroid

background containing lymphocytes. No epithelioid cell granuloma was present. Smears from case diagnosed as Non-seminomatous germ cell tumor showed cell clusters, trabeculae and papillaroid fragments of cells having high N/C ratio, irregular nuclear contours, inconspicuous nucleoli and moderate amount of cytoplasm with vacuolization in few.

In five cases, cytological diagnosis of Carcinoma [no specific type] was given. The smears showed pleomorphic nuclei, high N/C ratio, coarse chromatin, prominent nucleoli and moderate amount of cytoplasm and further morphological differentiation as squamous cell carcinoma/ adenocarcinoma/ neuroendocrine carcinoma on cytology could not be ascertained. Primary was not known in any of these cases

Out of the 39 cases in neoplastic category, histopathology was available in only 28 cases in which the cytological-histological correlation was done.

Out of the 28 cases, 2 cases were non representative on histopathology because of inadequate sampling (one case necrosis only and the other case fibrocollagenous tissue only on histopathology) and were excluded from cyto-histopathological correlation.

IHC was done in 24 cases where relevant markers were analysed which helped in reaching a final diagnosis.

**Table 26- Cyto-histopathological correlation of Neoplastic lesions [n=26]**

| **Cytohistopathological correlation** | **No.of cases** | **Percentage** |
|---|---|---|
| Concordance | 23 | 88.46% |
| Limited concordance | 03 | 11.54% |

**Table 27-Cyto-histopathological correlation of concordant cases (n=23)**

| Cytological Diagnosis | Histopathological diagnosis | Immuno-positive | Immuno-negative | Final diagnosis | No.of cases |
|---|---|---|---|---|---|
| Lymphoma (n=08) | Non-Hodgkin's lymphoma | LCA<br>MUM-1<br>Bcl-6<br>CD23<br>CD20(Diffuse)<br>Mib-1=98% | CD3 | Primary mediastinal large B-cell lymphoma | 02 |
| | | LCA<br>CD20<br>Mib1=70% | Bcl2<br>Bcl6<br>CD10 | NHL-large B-cell type | 02 |
| | Malignant round cell tumor | Tdt<br>CD3<br>CD8<br>CD5 | CD20<br>CD117<br>MPO | T-Lymphoblastic lymphoma | 02 |
| | Lymphoma | CD15<br>CD30 | LCA<br>CD20 | Hodgkin's Lymphoma-Classical type | 02 |
| Germ cell tumor (n=02) | Neoplasm | PLAP, OCT3/4 (strong &uniform ) | AFP<br>CK | Seminoma | 01 |
| | Germ cell tumor | SALL-4<br>AFP | PLAP<br>CD30 | Non-seminomatous germ cell tumor | 01 |
| Carcinoma (n=03) | Epithelial malignancy - Carcinoma | P63<br>CK5/6<br>CD117<br>p16<br>CD5<br>CK7(focal) | CK20<br>TTF-1 | Thymic carcinoma | 01 |
| | Epithelial malignancy - Carcinoma | - | - | Epithelial malignancy-Carcinoma | 02 |
| Malignant round cell tumor (n=03) | Neuroendocrine Tumor | CK<br>Chromogranin A<br>Synaptophysin<br>Mib-1= 80% | LCA | Neuroendocrine Tumor grade 3 | 01 |

| | | | | | |
|---|---|---|---|---|---|
| | Malignant round cell tumor | Synaptophysin<br>CK<br>Mib1=90% | LCA | Neuroendocrine tumor | 01 |
| | Malignant round cell tumor likely Small Cell Carcinoma | - | | Malignant round cell tumor likely SmallCell Carcinoma | 01 |
| Metastatic tumor (n=06) | Malignancy Neuroendocrine carcinoma01 | CK<br>TTF1<br>Synaptophysin<br>Chromogranin A<br>Mib-1=90% | LCA | Large cell neuroendocrine carcinoma-(lung) | 01 |
| | Neuroendocrine carcinoma | CK<br>CK7<br>p63<br>TTF-1<br>Chromogranin A (Dot like)<br>Mib-1=100% | CK20 | Large cell neuroendocrine carcinoma-(Lung) | 01 |
| | Neuroendocrine tumor | TTF-1<br>Synaptophysin<br>Mib1= 95% | | Neuroendocrine carcinoma-small cell type Primary from lung | 01 |
| | Carcinoma | CK<br>p40 | TTF-1<br>Chromogranin A<br>Synaptophysin | Squamous cell carcinoma (esophagus) | 01 |
| | SCC | CK<br>p63<br>CK5/6 | CK20<br>TTF-1<br>NapsinA | Squamous cell carcinoma (pleura) | 02 |
| Neuroblastic tumor (n=01) | Schwannian rich neuroblastic tumor | S100- positive in schwannian stroma<br>Synaptophysin,<br>NSE - positive in ganglion cells and schwannian stroma | Chromogranin A | Schwannian rich neuroblastoma | 01 |

All 10 cases of cytologically diagnosed lymphoma cases were subjected to histopathological evaluation and IHC studies. 8 of these cases were concordant, 2 showed limited concordance (Table-28). There were 6 cases of Non-Hodgkin's lymphoma, out of which 4 were of large-cell lymphoma (LCL), and 2 of T-lymphoblastic lymphoma (T-ALL) and 2 cases of Hodgkin's lymphoma both of classical type on histology.

Germ cell tumor was reported in 2 cases which were concordant histologically.In one case on IHC, the tumor cells were strongly and uniformly positive for PLAP and OCT3/4 and negative for cytokeratins and AFP and diagnosed as seminoma. Sections from case diagnosed as Non-seminomatous germ cell tumor, on IHC, the tumor cells were positive for SALL-4, AFP and negative for PLAP and CD30 hence diagnosed as Non seminomatous germ cell tumor.

Malignant round cell tumor were diagnosed in 4 cases, out of which histopathology was received in 3 and all of them were concordant (Neuroendocrine tumor)

Metastatic tumor were diagnosed in 9 cases cytologically out of which 6 cases biopsies were received and all of them are concordant.Metastatic Neuroendocrine tumor was cytologically diagnosed in 5 cases out of whichhistopathology was received in only 3 cases and in 2 cases primary was known (lung) and 1 case was of unknown primary.On histology and IHC, final diagnosis were 2 cases of large cell neuroendocrine carcinoma and 1 of neuroendocrine carcinoma - small cell type. Metastatic Squamous cell carcinoma was cytologically diagnosed in 4 cases out of which histopathology was available in 3 cases and 3 cases were concordant.

Carcinoma NOS was diagnosed in 5 cases cytologically, out of these histopathology were received in 3 cases and all 3 were concordant. 2 cases were given as carcinoma on histopathology and further IHC was not done in these cases for cell typing. One case was diagnosed as epithelial malignancy on histopathology and on IHC the tumor cells

were positive for P63, CK5/6, CD117, p16, CD5, CK7 (focal positive) and negative for CK20 and TTF1 . Final diagnosis of thymic carcinoma was given.

1 case of neuroblastic tumor was diagnosed cytologically which was concordant on histopathology. On IHC Synaptophysin, NSE were positive in ganglion cells and schwannian stroma and S100 was positive in schwannian stroma only. Hence final diagnosis of Schwannian rich neuroblastoma was given.

**Table 28-Cyto-histopathological correlation of cases with limited concordance [n=03]**

| **Cytological diagnosis** | **Histopathological diagnosis** | **Immunopositive** | **Immunonegative** | **Final diagnosis** | **No. of cases** |
|---|---|---|---|---|---|
| Large cell lymphoma | Malignancy | CK<br>Chromogranin A<br>Mib-1=90% | Synaptophysin<br>TTF-1 | Large cell Neuroendocrine Ca | 01 |
| Thymoma | Lymphoma possibly NHL | LCA<br>Bcl-6<br>CD23<br>CD20<br>Mib-1=90% | CD3 | Primary mediastinal large B-cell lymphoma | 01 |
| Hematolymphoid malignancy possibly lymphoma | Malignant round cell tumor | CK<br>EMA<br>CD99(membranous)<br>Mib-1=50% | LCA | Primitive neuroectodermal tumor (PNET) | 01 |

In three cases though the category of ‘Neoplastic’ was concordant on histo-cytological correlation it was of limited nature as the specific diagnosis did not match. Two cases were diagnosed as lymphoma on cytology and on histopathology and IHC they were diagnosed as PNET and large cell neuroendocrine carcinoma and in one case on cytology it was diagnosed as thymoma but further on histopathology and IHC it was diagnosed as primary mediastinal large B cell lymphoma.

# DISCUSSION

The mediastinum is an extremely complex region of the human body.Mediastinal lesions represent a wide diversity of disease states in view of multiplicity of the anatomical structures located in this area. An accurate and early tissue diagnosis is warranted in mediastinal lesions to separate malignant lesions from the nonneoplastic and benign conditions as the treatment goals are different. These lesions often pose diagnostic problems because of their location and difficult access. Diagnosis of mediastinal lesions has been a challenging task for all radiologists and pathologists since it has been considered as a “Pandora’s box” within which congenital cysts, benign tumors, primary and metastatic neoplasms develop. Mediastinal masses can be neoplastic, congenital, inflammatory, hematopoietic, metastatic or vascular in origin. Mediastinal mass can be asymptomatic or produce a wide range of non-specific symptoms, breathlessness and vague chest pain.

Fine needle aspiration cytology (FNAC) is a relatively non-invasive technique that can be used alone or in conjunction with core needle biopsy prior to therapy, allows for diagnosing the lesion besides rapid on-site evaluation, and is helpful in triaging material for ancillary studies such as flowcytometry, immunohistochemistry, and molecular studies. In order to prevent open surgical exploration, fineneedle aspiration cytology (FNAC) under ultrasound (USG) or computed tomography (CT) scan guidance and EUS guided FNAC has been used increasingly and successfully to resolve the diagnostic dilemmas.

The present study was undertaken to study the cytological spectrum of mediastinal lesions by FNACs in a tertiary care hospital. It was a 5 years study from 1$^{st}$ July 2016 - 30$^{th}$ June 2021 (3.5 years retrospectively and 1.5 years prospectively). All the patients who underwent image guided FNA from mediastinal lesions were included in the study. In each patient clinical and radiological findings were

recorded. Cell block findings and histopathological findings with IHC were correlated with cytological findings wherever possible.

Out of a total of 9,088 FNACs analysed in the Department of Pathology from 1st July 2016 - 30th June 2021, 102 cases were from mediastinum (1.12%) which were analysed in this study. Histopathological correlation was done in 36 cases out of 102 cases.

The most common age group undergoing mediastinal FNAC was 51-60 as also seen by Pandey DK et al.[74] The age ranged from 2 years to 81 years, with a mean age of 46.63 years also seen by Assad et al.[73] Mean age wise distribution of various studies are described in table below:

**Table 29: Mean age wise distribution of various studies**

| **Studies** | **Mean age** |
|---|---|
| Dasgupta S et al[5] | 18.3 years |
| Karki and Chalise[86] | 35.5 years |
| Dixit R et al [84] | 45.5 years |
| Assaad et al[73] | 57 years |
| Shabb et al[72] | 41 years |
| Dalal UR et al[79] | 33.6 years |
| Choudhuri et al[81] | 47 years |
| Pandey DK et al[74] | 52 years |
| Sharma P et al[80] | 37.5 years |
| Present study | 46.6 years |

Variation in the mean age in different studies is attributed to the fact that some studies were focussed mainly on infant and pediatric age group, moreover number of study patient included is also an additional factor accounting for this variation.

In the present study, male patients contributed 59.80% of all the cases, whereas females constituted 40.20% of the cases. Thus a male predominance with a male to female ratio of 1.4:1 was noted. This is in concordance with other studies that have also reported male preponderance and described below.

**Table 30: Sex wise distribution of various studies**

| Studies | Male to female ratio |
|---|---|
| Choudhuri et al[81] | 2.6:1 |
| Goel et al[75] | 2:1 |
| Dasgupta et al[5] | 2.1:1 |
| Shabb et al[72] | 1.4:1 |
| Dubashi et al [87] | 2.8:1 |
| Assad et al[73] | 1:1.1 |
| Dixit R et al[84] | 5:1 |
| P. Sharma et al[80] | 2:1 |
| Present study | 1.4:1 |

In our study, fever and cough were the most common presenting clinical symptoms seen in 43.14% of the patients. These were followed by loss of weight, dyspnea, loss of appetite and chest pain. Our findings are similar to observations made by P. Sharma et al[80], Dubashi et al[87], Dixit R et[84] and Choudhuri et al[81] who found that 96.8%, 97%, 95.3% and 96% respectively of the patients were symptomatic at presentation and the most common symptom reported was cough followed by chest pain, dyspnoea and weight loss. Dasgupta S et al,[5] also found all patients complaining of chest pain and dyspnea. Shabb et al[72] and P Sharma et al[80], also found most common symptoms were dyspnea, cough and chest pain.

A total of 102 patients had mediastinal masses involving different compartments of the mediastinum. On subdivision of the masses into separate compartments, it was found that 60 patients had masses in anterior /superior mediastinum, ie 58.8%; 33 patients had masses in

middle mediastinum ie 32.35% and 7 patients had masses in posterior mediastinum ie 6.86% and in 2 cases (1.96%) two compartments of mediastinum were simultaneously involved . Similar findings were seen in a study by Dixit R et al[84],Pandey DK et al[74], Shrivastava PC et al [88] and Abebe Bekele et al [89]

**Table 31: Compartment wise involvement in various studies**

| Studies | Anterior/ Superior | Middle | Posterior | More than 2 compartments |
|---|---|---|---|---|
| P.Sharma et al[80] (n=60) | 22 (36.7%) | 20 (33.3%) | 18 (30%) | |
| Dasgupta S et al[5] (n=22) | 10 (45.5%) | 7 (31.8%) | 5 (22.7%) | |
| Dixit R et al[84] (n=139) | 95 (68.3%) | 23 (16.5%) | 11(2.5%) | 10 (7.1%) |
| Pandey DK[74]et al (n=48) | 30 (62.5%) | 16 (33.3%) | 02 (4.16%) | |
| Abebe Bekele et al[89] (n=73) | 45 (61.6%) | 05 (6.8%) | 23 (31.5%) | |
| Shrivastava PC et al[88] (n=106) | 76 (72%) | 13 (12%) | 17 (16%) | |
| Present study (n=102) | 60 (58.8%) | 33(32.35%) | 07 (6.86%) | 2 (1.96%) |

All the cases in our study were divided into 3 categories non-neoplastic, neoplastic and non-diagnostic for evaluation constituting 34.31%, 38.24% and 27.45% of all the cases respectively. The neoplastic cases constituted majority of cases as also seen in in various studies as described in the table below. However, this is in contrast to study by, Dalal UR et al[79] who reported majority of the cases were non-neoplastic in nature as described in table below:

**Table 32: Distribution of mediastinal lesions category wise by various studies.**

| Studies | Non-neoplastic | Neoplastic |
|---|---|---|
| Dixit R et al[5] | 23% | 66.9% |
| Choudhuri et al[81] | 24% | 68% |
| Aassad et al[73] | 10.1% | 67.9% |
| Shabb et al[72] | 12% | 81% |
| Pandey DK et al[74] | 21.4% | 64.3% |
| Goel et al[75] | 21.5% | 78.5% |
| Dalal UR et al[79] | 68.9% | 31.0% |
| Present study | 34.31% | 38.24% |

In our study, granulomatous inflammation was the predominant pattern seen in 27 cases (26.47%) which included tuberculosis (n=08) with ZN stain for AFB positive and culture positive cases. Kaur et al.[84] reported tuberculosis in 33.3% cases and Shaheen et al[84]in 5% cases, whereas Adler et al[84] reported tuberculosis in none of their patients. This gross difference in the occurrence of tuberculosis is probably due to low prevalence of tuberculosis in western countries compared to developing countries.

In our study, amongst all the cases analysed , there were 3 cases (2.94%) of reactive hyperplasia of lymph node, 2 cases (1.96%) of benign cystic lesion, 2 (1.96%) of acute suppurative pathology and 1 case (0.98%) of non-specific inflammation of mediastinal Lymph node. A study by Goel et al[75] found one case having suppurative inflammation with neutrophils, and the smears were negative for AFB and fungal stains.

Neoplastic category included 39 out of a total of 102 cases (38.23%) and the most common age group in this category was 51-60 years. Neoplastic lesions were found to present clinically two decades later then the patients belonging to the non neoplastic category in our study. This finding is in concordance with study done by Powers et al. [90]who

showed increased prevalence of neoplasm after age 50 years, with average age of 54 years;

Neoplastic lesions were more common in males (74.35%) than in females (25.64%) in the present study which is in concordance with Choudhuri et al[81] who also reported male predilection in neoplastic lesions.

In our study, lymphoma constituted 11.76% of all cases followed by metastatic deposits which constituted 8.82% of cases. This isin concordance to study done by Shrivastava et al.[88] and Shabb et al[72] where lymphoma and metastatic tumors were also common. Dixit R et al[84] found 19.3% of cases of lymphoma. Goel et al[75]found 26.5% cases of lymphoma. Pandey DK et al[74] found 12.5% cases of lymphoma, Dasgupta S et al[5] found 22.7% cases of lymphoma.

Adler et al. and Assaad et al[73] showed an appreciable proportion of metastatic lesions in the mediastinum (48% and 45%, respectively). These findings are similar to study by Nasit et al.[78]who also observed metastatic malignant lesions in 38% of their series. These variations may be contributed by difference in the number of patients, age range in different studies and geographical variation.

In our study, metastatic tumors accounted for 8.8% of cases. There was mediastinal invasion by either squamous cell carcinoma and neuroendocrine carcinoma. There was one case of metastatic adenocarcinoma from GIT on histopathology and IHC but the aspirate material was inadequate on FNAC. Our findings are similar to those in study done by Choudhuri et al[81] who found 4 cases of metastatic squamous cell carcinoma and 2 cases of metastatic adenocarcinoma. Shabb et al[72] found 24% metastatic tumors (9 cases of carcinoma and 1 sarcoma)

In our study, thymic lesions constituted (4.9%) of all the cases. There were 4 cases of thymoma and one case of thymic carcinoma. Karki

and Chalise[86] (20.1%), Goel et al[75] (12.7%), Assad et al[73](6.25%) , Shabb et al[72] (7.1%) have reported higher percentage of thymic lesions in their studies, while Dixit R et al.[84]have found only 3.5% of their cases as thymic lesions.

In present study, there were 2 cases of germ cell tumors(1.96%), one was seminoma and other was of non-seminomatous GCT. This is in concordance to study done by P Sharma et al[80]where Germ cell tumours were seen in 4 cases (6.66%). They reported two cases of classical seminoma, 1 of mature teratoma and other was diagnosed as mixed germ cell tumour. Dasgupta S et al[5]found 3 cases of GCT (one of mixed GCT, one of mature cystic teratoma and one of dysgerminoma) Dalal UR et al[79] found 6 cases of teratoma but in our study we did not find any case of teratoma and dysgerminoma.

In our study, a single case of neuroblastoma was seen in posterior mediastinum which is in concordance with study by Karki and Chalise,[86] Goel et al[75], Dalal UR et al[79]. Other studies like Goel et al[75], Dixit R et al[84] reported cases of sarcoma but in our study we did not find any case of sarcoma.

In this study, one case was incorrectly diagnosed as thymoma on FNAC which was diagnosed as Non-Hodgkin lymphoma on histopathology and IHC. This discrepancy occured because the aspirate was scanty and aggregates of histiocytes were misinterpreted as epithelial component of thymoma while lymphocytes were interpreted as lymphocytic component. Similar dilemma was also faced by Shabb et al.[72] and Assad et al.[73]

In our study, there was one case where distinction between poorly differentiated carcinoma and lymphoma was not made. Similar challenge was also faced by Shabb et al.[72] In one case Lymphoma was diagnosed on cytology and on HPE and IHC, it was turned out to be PNET. Similar dilemma was faced by Pandey DK et al.[74]

In our study, 28 cases (27.45%) were non-diagnostic for evaluation. Two cases had no diagnostic material, 18 had scanty cellularity and 08 were unsatisfactory due to blood obscuring the cells. Similar factors were responsible for unsatisfactory smears in a various studies as described below .The failure to achieve diagnosis by FNAC may be contributed by several factors, i.e., sampling error leading to scanty material, poor smear preparation, poor cooperation of the patient, dense fibrosis and extensive necrosis etc.

**Table 33: Percentage of non-diagnostic cases in various studies**

| Studies | Non diagnostic cases |
|---|---|
| Dixit R et al[84] | 10% |
| Shabb et al[72] | 7% |
| Karki and Chalise[86] | 7.4% |
| Pandey D K et al[74] | 14.3% |
| Nasit et al[78] | 8% |
| Adler et al[84] | 11% |
| Assaad et al[73] | 18% |
| Goel D et al[75] | 19.3% |
| Present study | 27.45% |

In many studies, making a specific diagnosis is not possible by FNAC, and only a classification into “malignant cells” or “non malignant cells” will be achieved. FNAC may suggest a diagnosis of lymphoma, but differentiation between Hodgkin’s disease, NHL, and thymoma can be difficult. In such instances either CNB from representative site or wide excision biopsy is required for special tests like IHC or molecular studies, cytogenetics. A major advantage of FNAC is that immediate cytological examination of the specimen is possible and then pathologist can direct the clinician appropriately for further diagnostic and treatment modalities.

Cytological-histological correlation was found in 36 cases out of 102 (35.29%) cases in our study. Almost similar concordance have been noted in studies by Pandey DK et al[74]in which the cytology and histopathology correlation was done in 20 cases out of 56 cases (35.7%). In another study by Dixit R et al[84] cyto-histogical correlation was done in 21 cases out of 104 (20.1%)cases.

As histological correlation was not available in all of our cases, so sensitivity could not be measured accurately. This lack of histopathology sample can be due to the fact that many patients are directly subjected to treatment solely based on the FNAC diagnosis because the clinicians rely on FNAC diagnosis. Surgical excision is not done in many cases like tuberculosis or inflammation where clinicians rely heavily on the clinic-radiological and cytological findings.

Overall no major complication was observed among the patients undergoing image guided mediastinal FNAC in our study. The strikingly low rate of complications can be explained by the fact that in our centre immediate on site cytological assessment is done which ensures minimum number of passes are made in mediastinal FNAC.

Thus from our study we can conclude that FNAC is simple, rapid and cost effective method for diagnosis of mediastinal lesions. It can be easily practiced in any centre, where specialized radiologists and pathologists are available. It can reduces patient's stay in hospital and thus the cost of treatment is also markedly reduced. FNAC has a good diagnostic accuracy so it is ideal as the first line of investigation in any mediastinal lesion, and can guide the clinician for prompt treatment and further prognostication.

# SUMMARY & CONCLUSION

A study of 102 patients who had undergone image guided fine needle aspiration (FNAC) of mediastinal lesions over a period of 5 years from 1st July 2016 - 30th June 2021 (3.5 years retrospectively and 1.5 years prospectively) was conducted in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana. In each patient clinical, radiological and serological findings were recorded. Correlation with histopathology and IHC was done wherever possible. Histopathological correlation was available in 36 cases. The following conclusions were found:

1. Mean age was found to be 46.63 years with youngest patient being 2 years old and oldest being 81 years old. Maximum cases were found to be in the age group of 51-60 years (27.45%).
2. Slight male preponderance was seen with M:F ratio of 1.4:1.
3. Fever and cough were the most common presenting symptom (43.14%).
4. Ultrasound guided aspiration followed by endoscopic ultrasound guided aspiration was the mostcommonly employed technique.
5. The most common radiological presentation was mediastinal mass (54.90%)
6. Anterior and superior mediastinum were the most commonly involved mediastinal compartment by various lesions accounting for 58.82% [n=60]
7. The lesions were categorized on cytology under the following categories: Non diagnostic (27.45%), Non neoplastic (34.31%) and Neoplastic (38.24%),
8. Non neoplastic cases constituted 34.31% of the total cases.
9. Major etiology amongst all cases was found to be Granulomatous inflammation accounting for 26.47% (n=27) of all mediastinal lesions with a definitive diagnosis of TB in 15.68% (n=16) of all cases.
10. Neoplastic lesions comprised 38.24% of total number of cases. Of the neoplastic lesions lymphoma (30.76%) followed by metastasis

(23.07%) was the most common. Thymoma accounted for 10.25% of neoplastic cases.

11. Non diagnostic accounted for 27.45% of cases with poor cellularity, obscuring factors and poor preservation being the root cause.
12. Cytohistological correlation was possible in 36 cases (35.29%).
13. Accurate categorization of lesions into non-neoplastic and neoplastic lesions was possible in 100% of cases and limited concordance within the neoplastic category was seen in 11.54% of cases.

**Conclusion:**

FNAC proved to be highly precise in categorizing mediastinal lesions into neoplastic and non-neoplastic categories in our study, however, it had few inherent limitations in subtyping certain neoplastic lesions and sample adequacy. In this era of precision medicine, ancillary techniques are essential for accurate typing, hence FNAC when done in conjugation with core needle biopsy should be regarded as complementary diagnostic processes in combination with clinical, radiological and other laboratory data.

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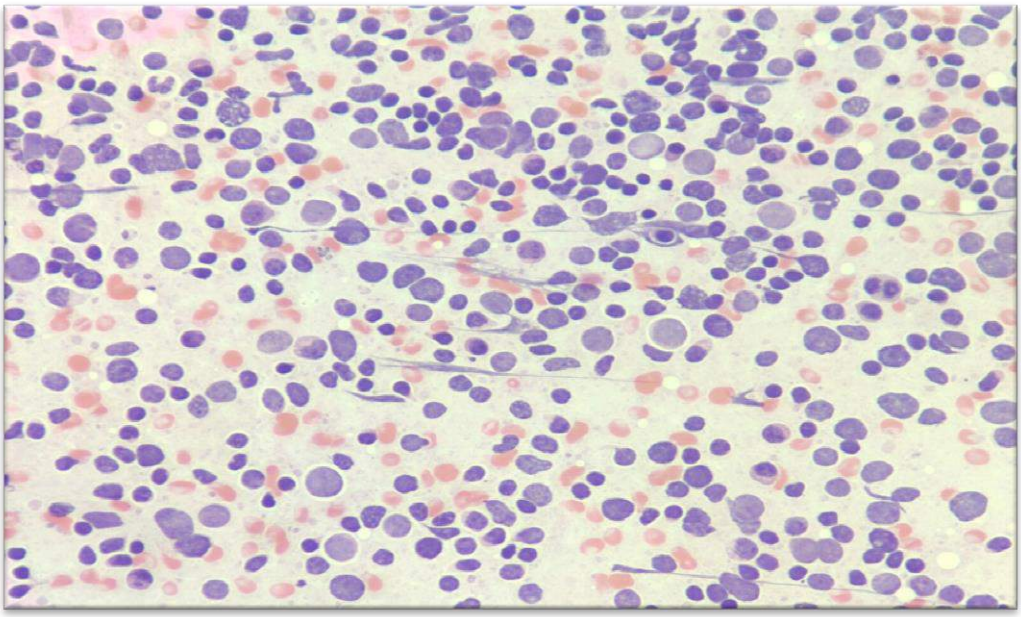

Figure 1**: Reactive hyperplasia -Mediastinal lymph node-** Cytological smear shows reactive lymphoid cells in varying stages of maturation. (H&E, 100X)

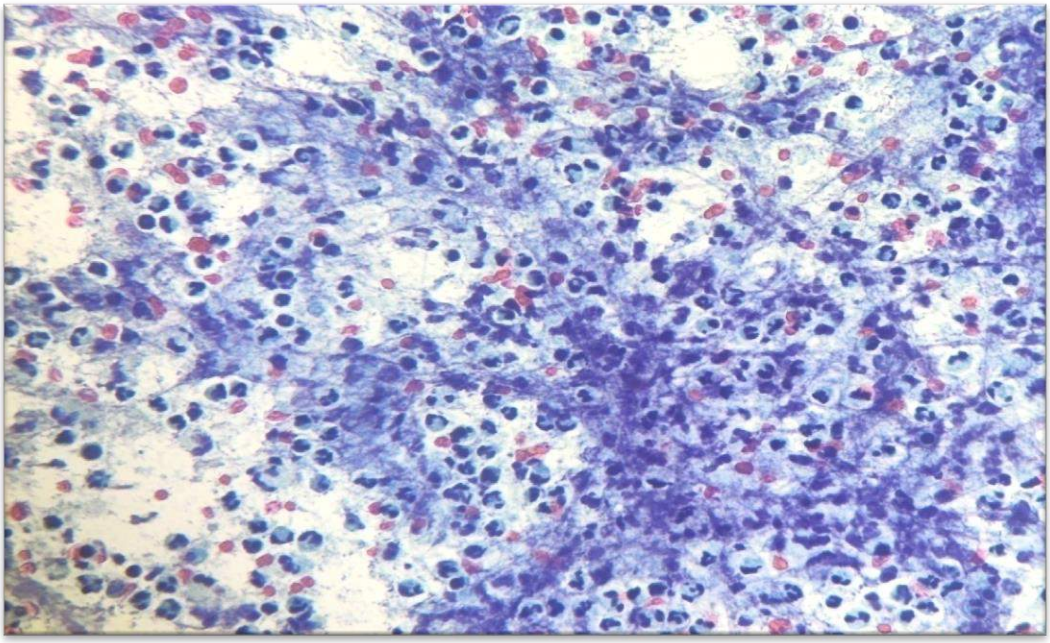

Figure 2**: Acute suppurative pathology- Abscess-** Cytological smear shows extensive areas of necrosis with degenerated and viable inflammatory cells seen as sheets of neutrophils along with few lymphocytes and foamy macrophages.(PAP,400X)

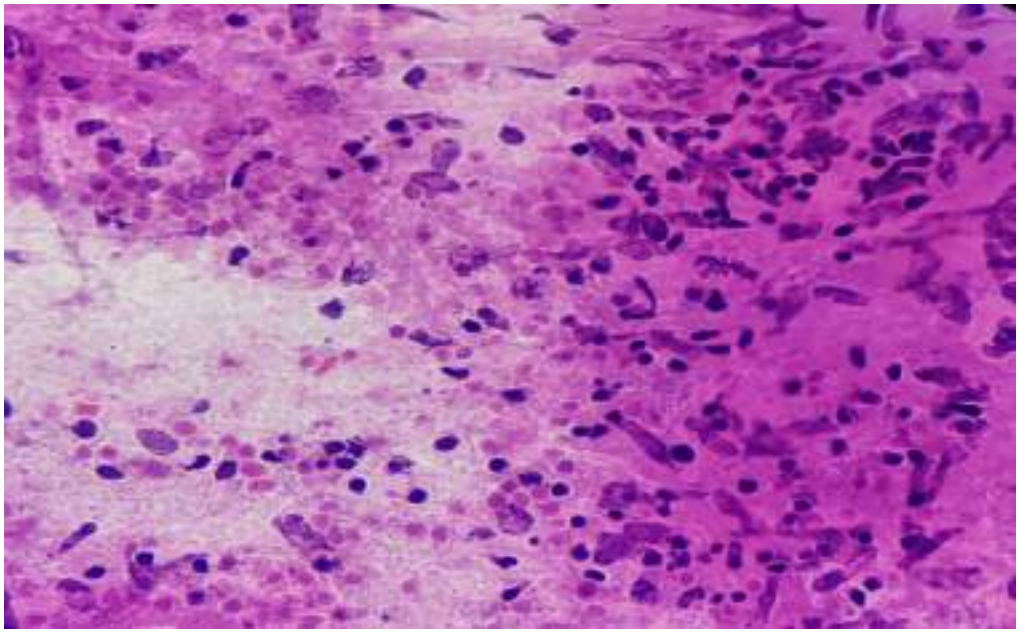

Figure 3**: Granulomatous inflammation - Mediastinal Lymph node-** Cytological smears shows epithelioid cell granulomas against necrotic background (H&E, 400X)

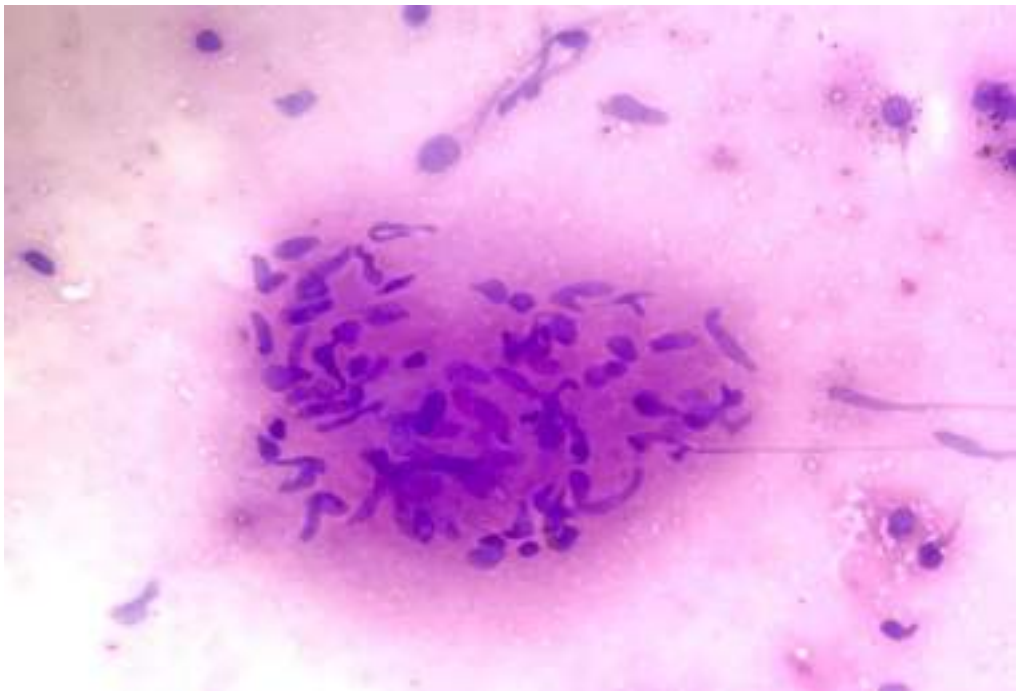

Figure 4: **Granulomatous inflammation - Mediastinal lymph node -** Cytological smears shows epithelioid cell granulomas (H&E, 400X)

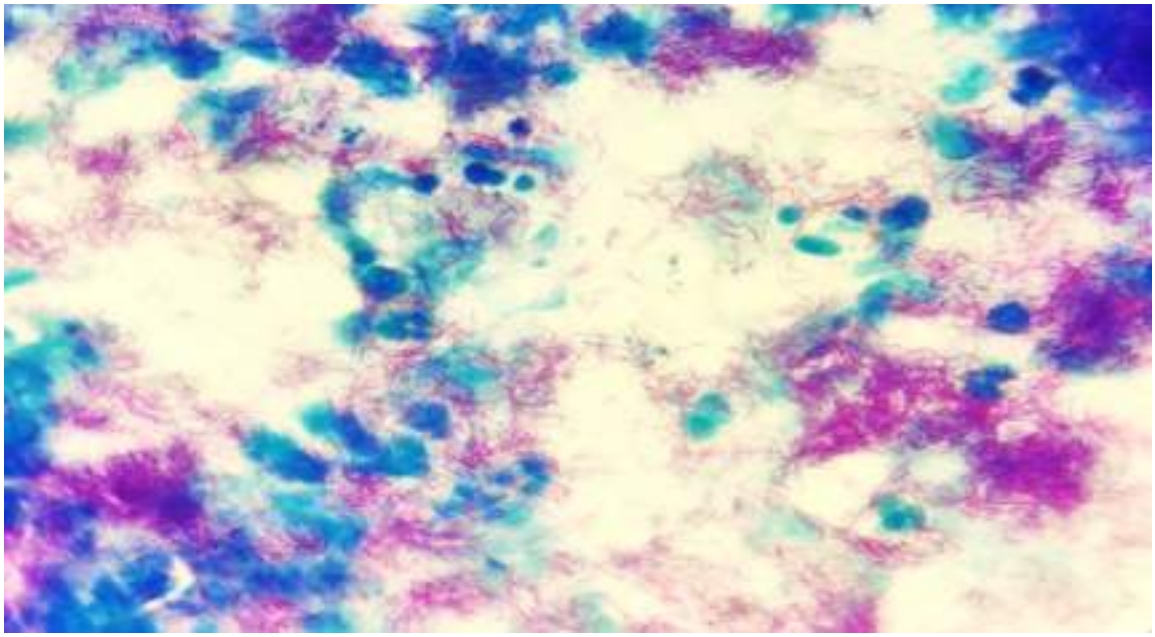

Figure 5: **Granulomatous inflammation consistent with Tuberculosis** - **Mediastinal lymph node**- Cytological smears shows numerous beaded acid fast bacilli (20% ZN stain, 1000X)

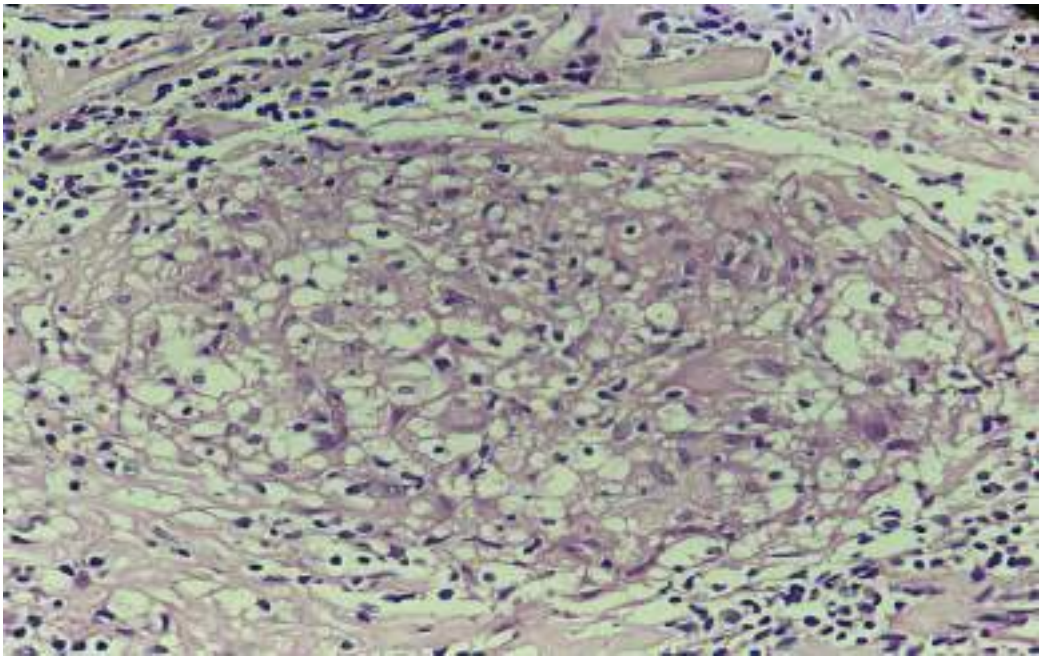

Figure 6**: Granulomatous inflammation - Mediastinal lymph node** - Histological section shows presence of well formed epithelioid cell granuloma surrounded by lymphocytic collar (H&E, 400x)

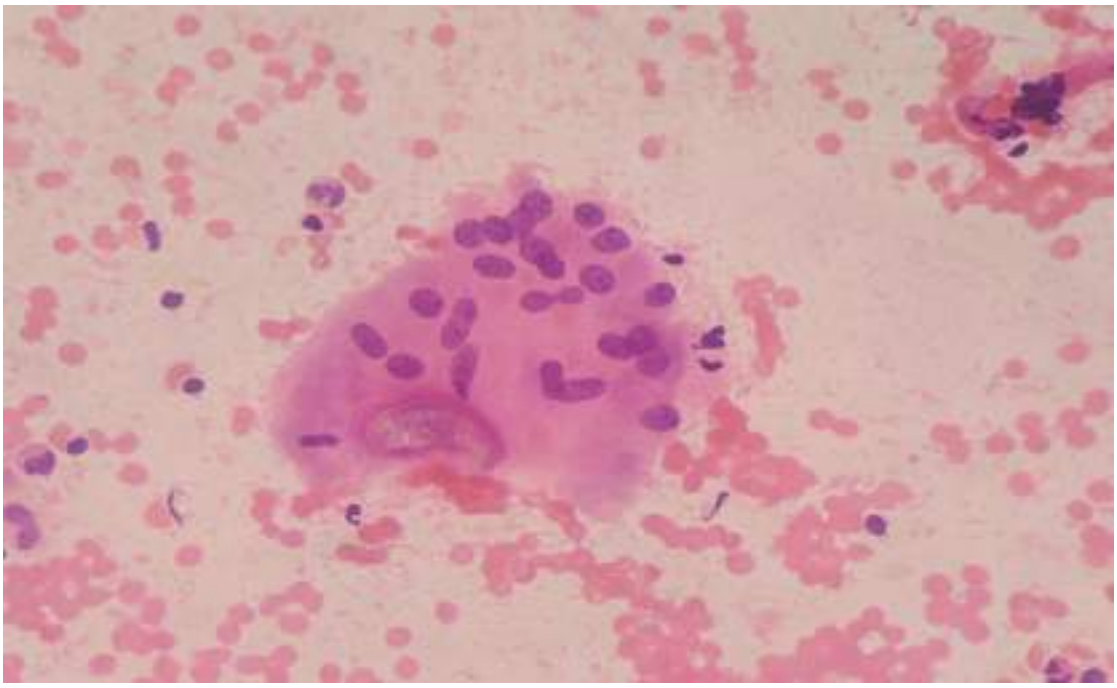

Figure 7**: Sarcoidosis - Mediastinal lymph node-** Cytological smear shows Schaumann body within multinucleated giant cell. Epitheloid cell granuloma seen in the vicinity. (H&E,400X)

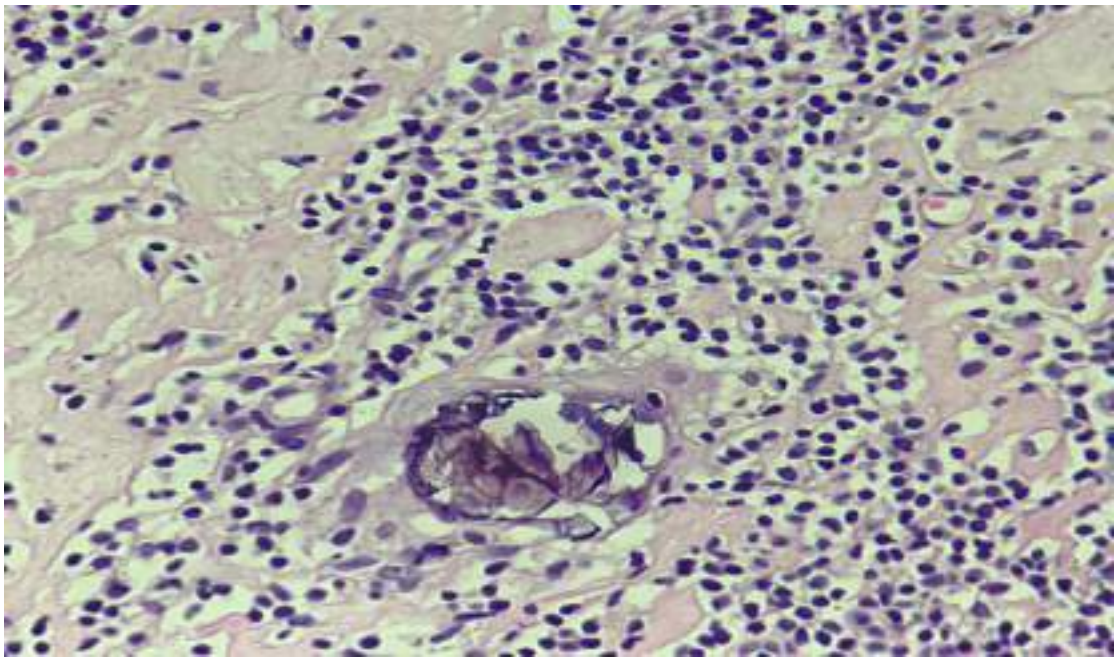

Figure 8: **Sarcoidosis - Mediastinal lymph node-** Histological section shows Schaumann body within multinucleated giant cell (H&E,400X)

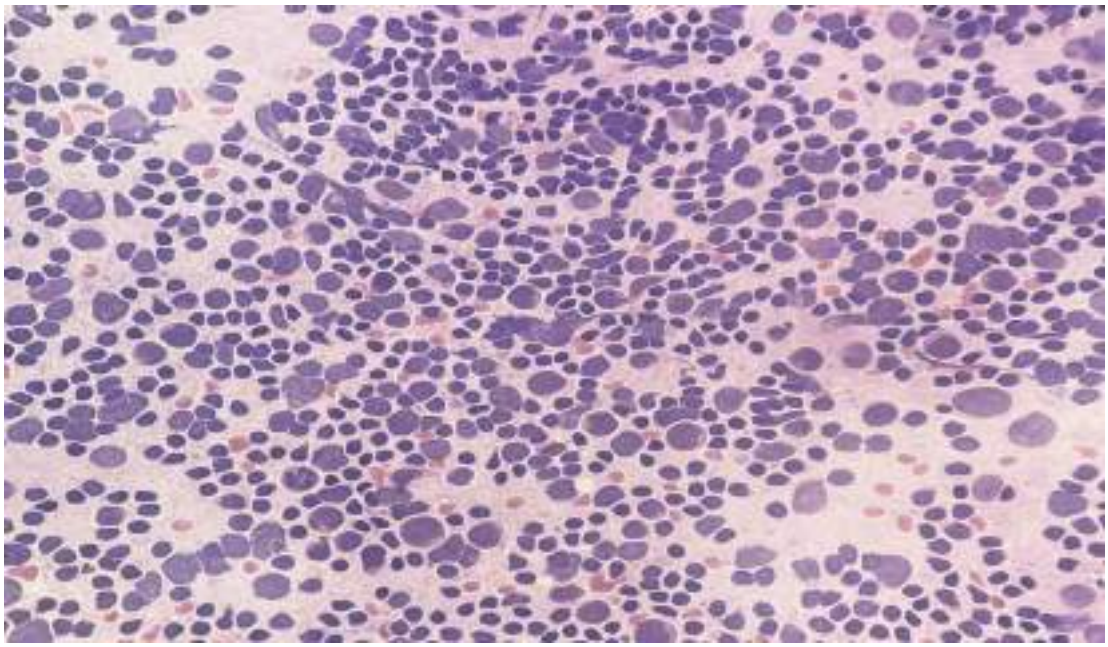

Figure 9: **Lymphoma Anterior mediastinal mass –** Cytological smears shows atypical lymphoid cells exhibiting high N/C ratio, nuclear pleomorphism, prominent nucleoli & scant cytoplasm. (MGG,100X)

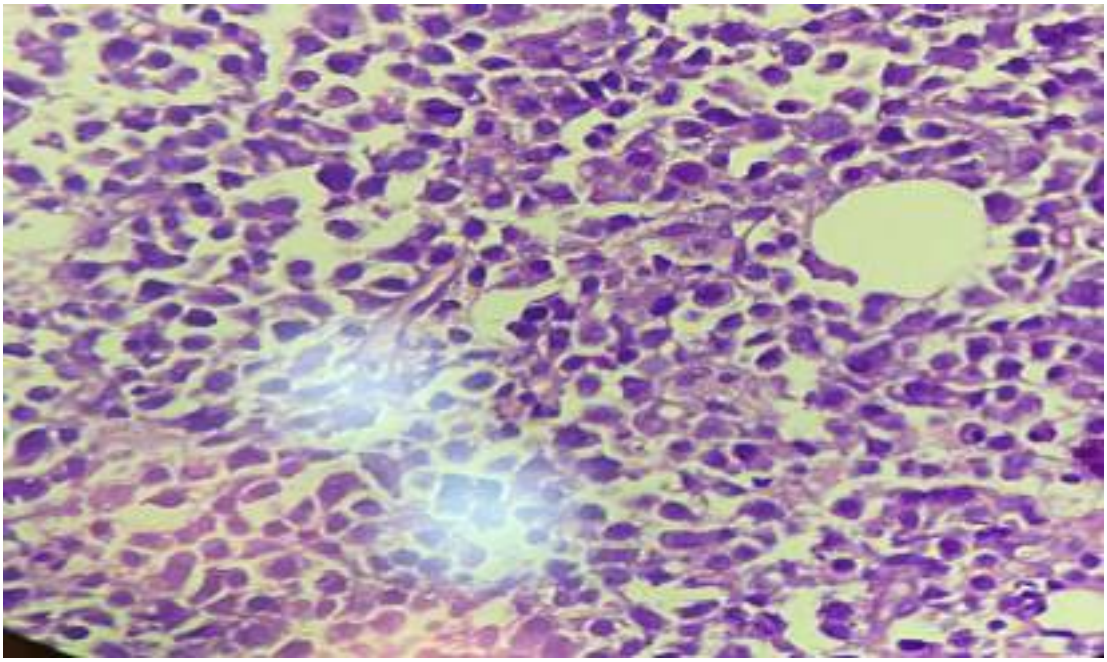

Figure 10: **Lymphoma- Anterior mediastinal mass –-**Histological section shows large lymphoid cells with inconspicuous nuceloli and scanty cytoplasm. (H&E,100X)

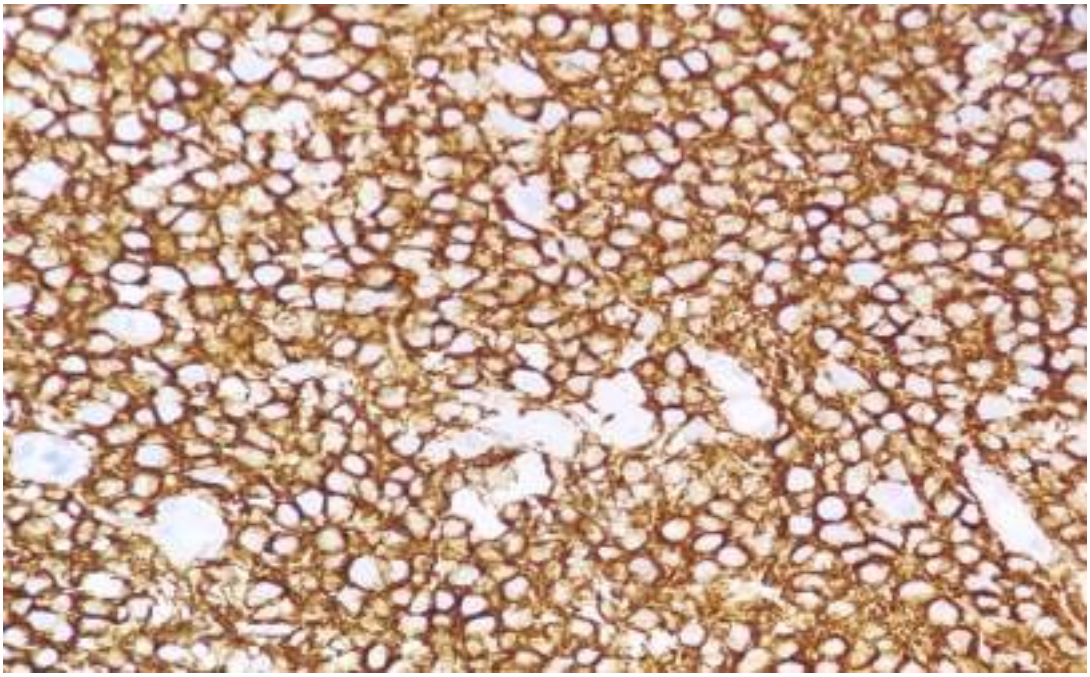

Figure 11: **Non Hodgkin Lymphoma- B cell type-** section show atypical lymphoid cells showing diffuse and strong immunoreactivity of CD20 (IHC, 400X)

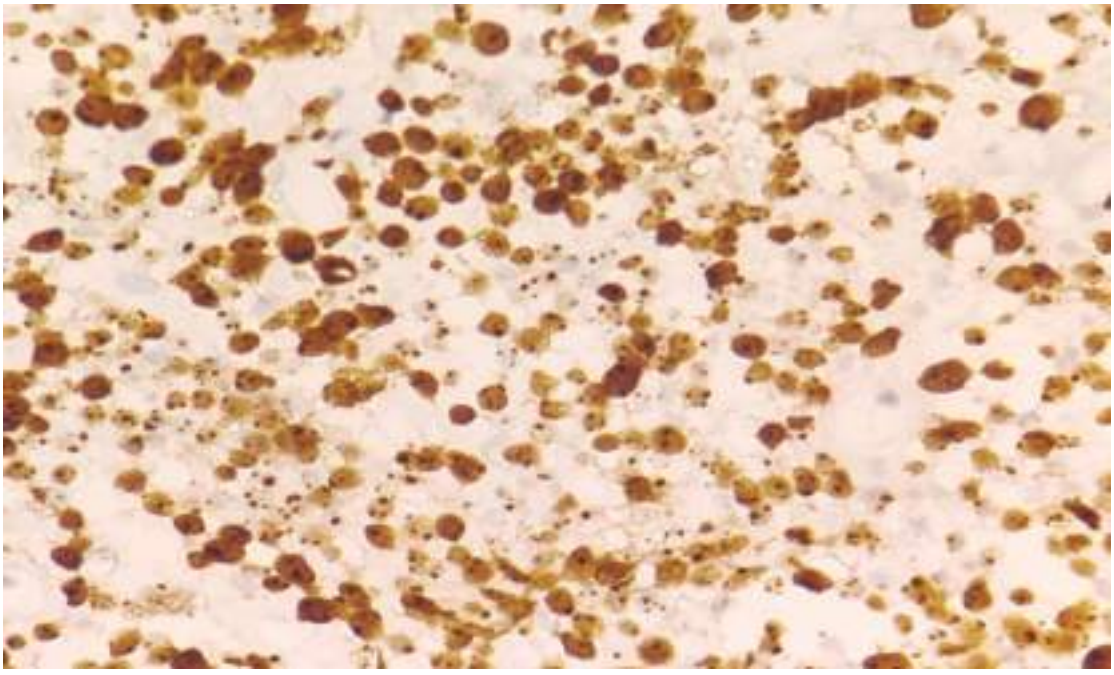

Figure 12: **High Grade Non Hodgkin Lymphoma-B cell Type--**Ki-67 proliferation index 80% (IHC, 400x)

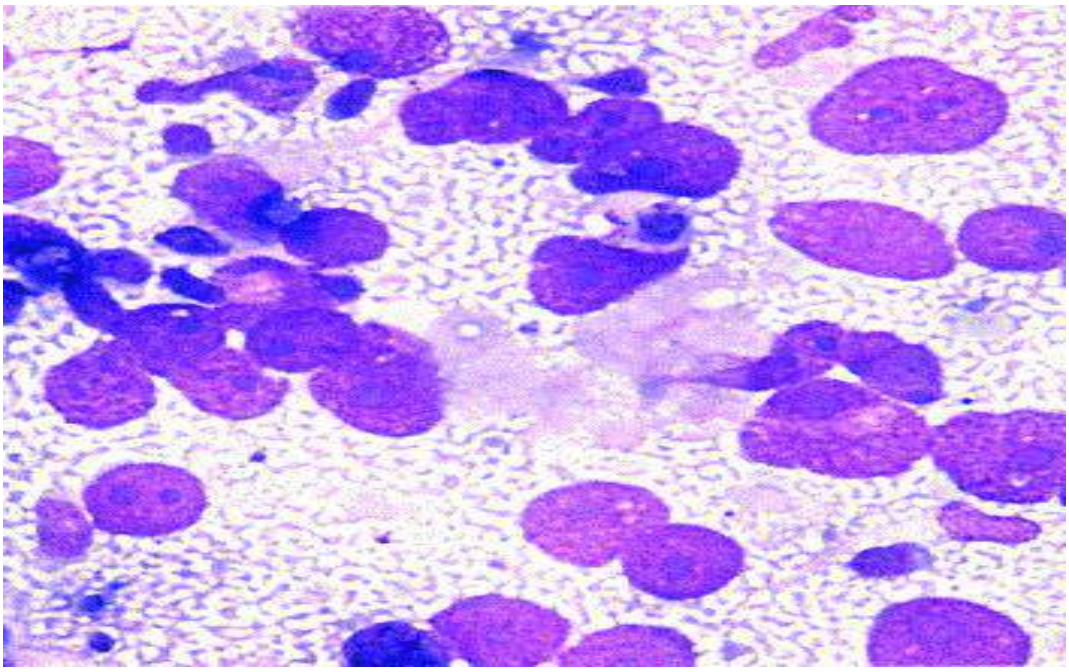

Figure 13**: Germ cell tumor, Seminoma-** Cytological smears shows atypical cells with large nuclei, macronucleoli and fragile cytoplasm against a tigroid background.(MGG,400X)

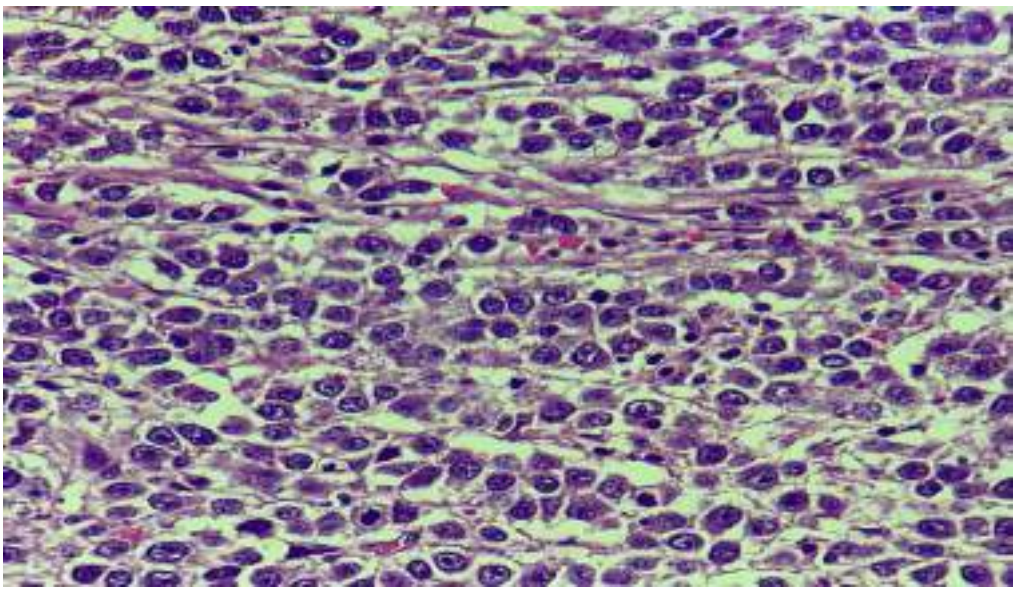

Figure 14: **Germ cell tumor, Seminoma-** Histological section shows tumor cells arranged in sheets having central nucleus, prominent nucleoli and moderate clear cytoplasm separated by fibrovascular septa infiltrated by lymphocytes. (H&E, 400X)

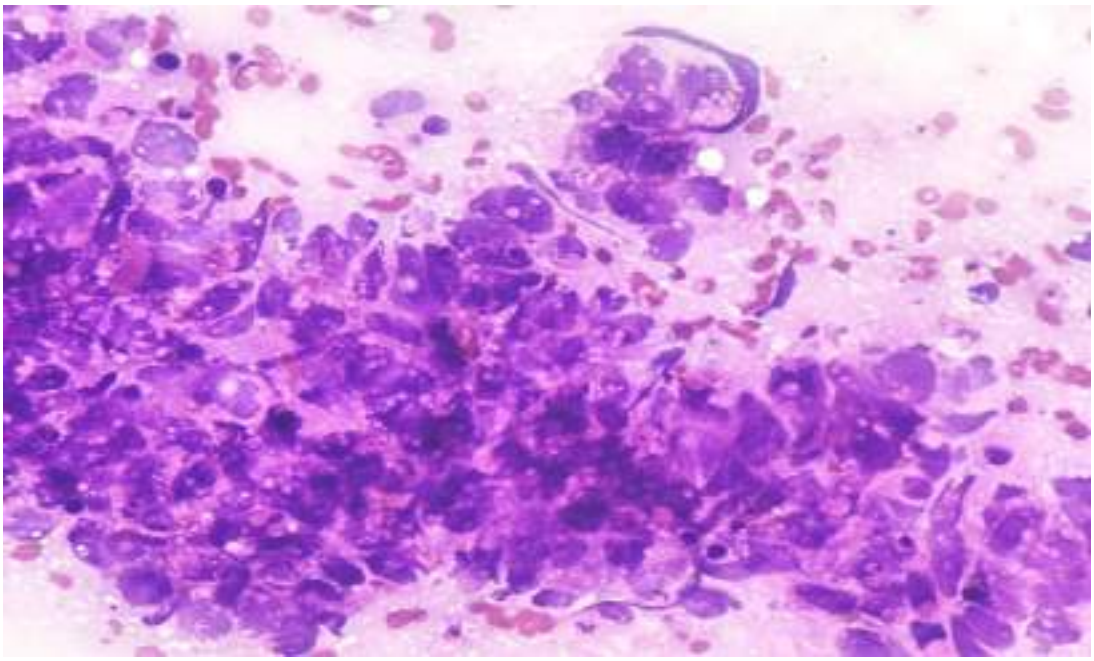

Figure 15: **Non-seminomatous Germ cell tumor-** Cytological smears shows clusters and papillaroid fragments of cells having high N/C ratio, irregular nuclear contours, inconspicuous nucleoli and moderate amount of cytoplasm with vacuolization in few. [H&E, 100X)

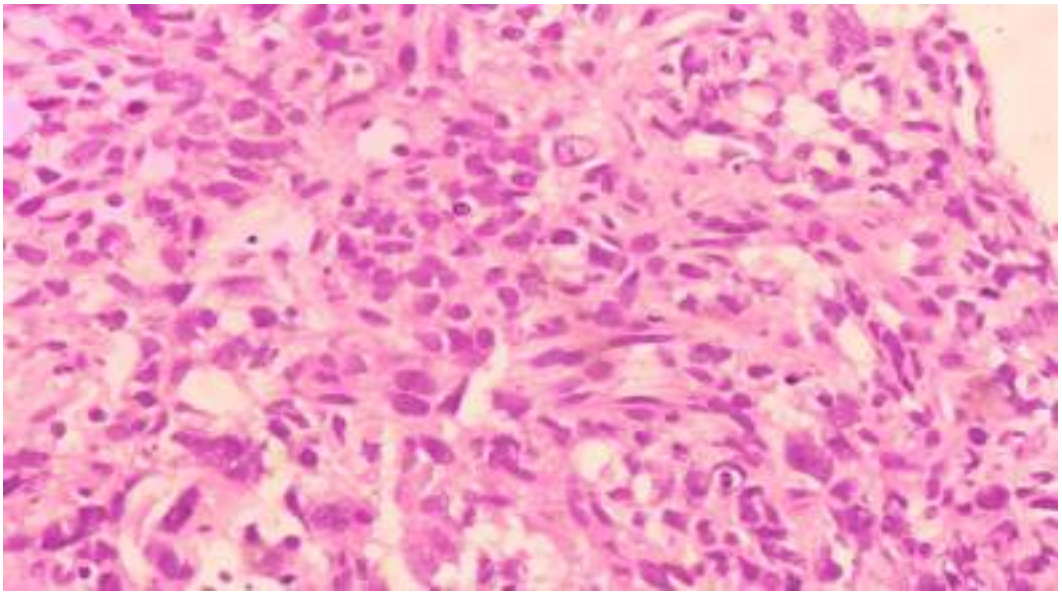

Figure 16**: Non-seminomatous Germ cell tumor-** Histological section shows tumor cells having oval vesicular nuclei , inconspicuous nucleoli and moderate amount of vacuolated cytoplasm. (H&E, 100X)

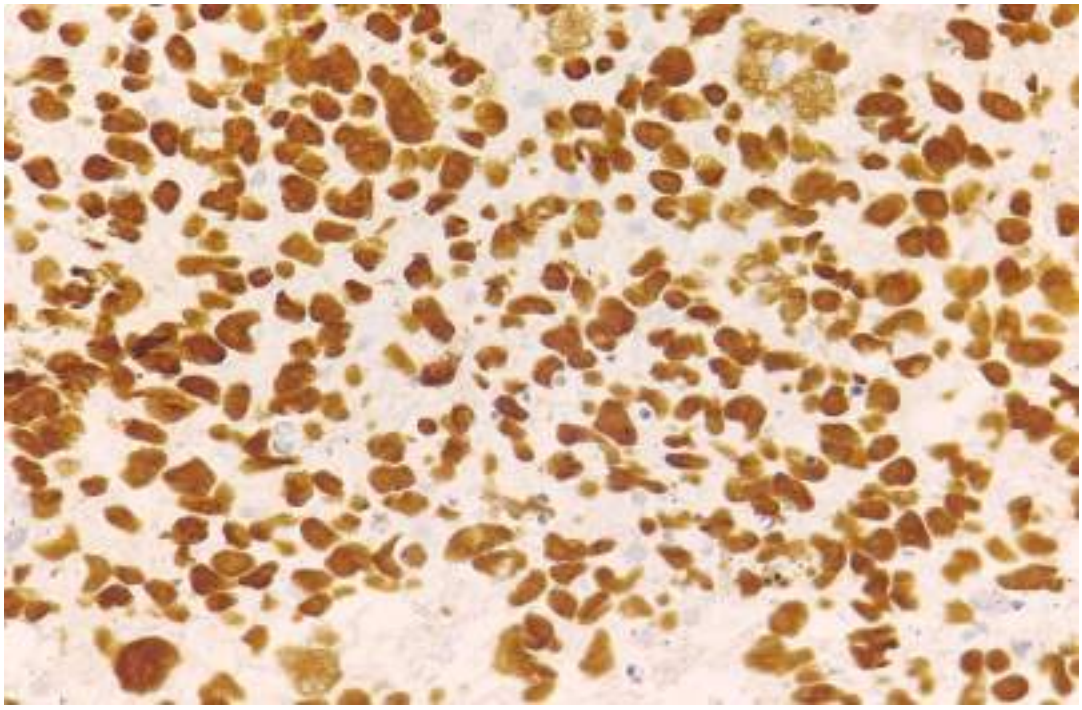

Figure 17: **Non-seminomatous Germ cell tumor-** Cells showing diffuse strong nuclear immunoreactivity of SALL4 (IHC, 400x)

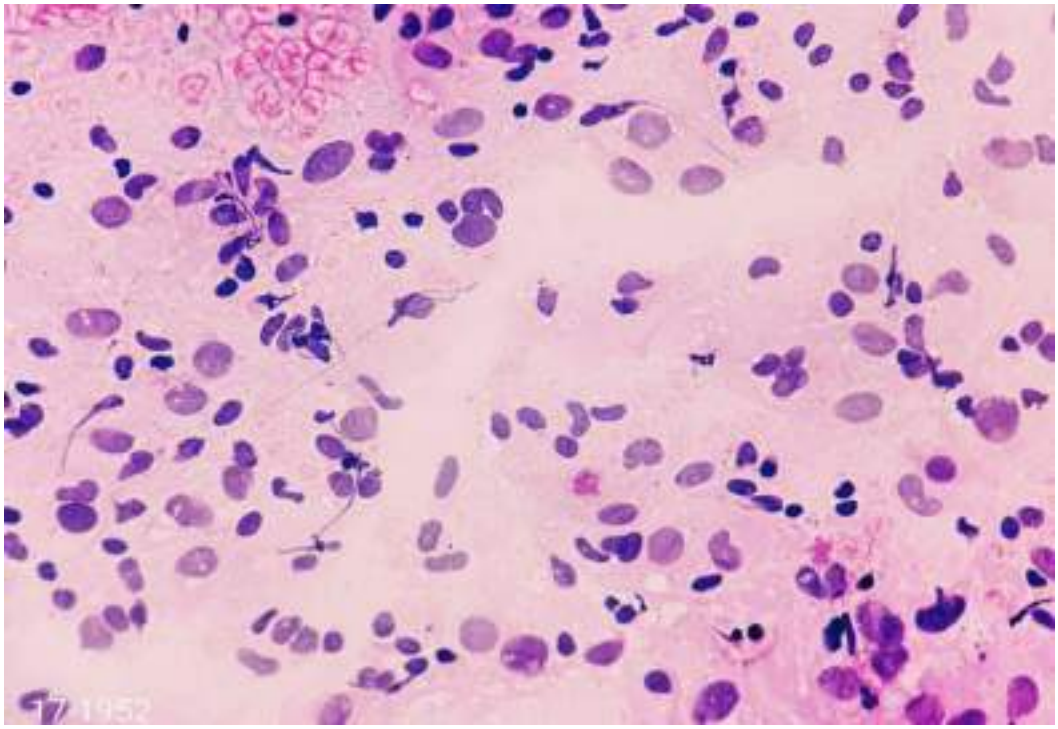

Figure 18**: Thymoma-** Cytological smears shows singly dispersed spindle to oval mildly pleomorphic cells having inconspicuous nucleoli and moderate cytoplasm (H&E,400X)

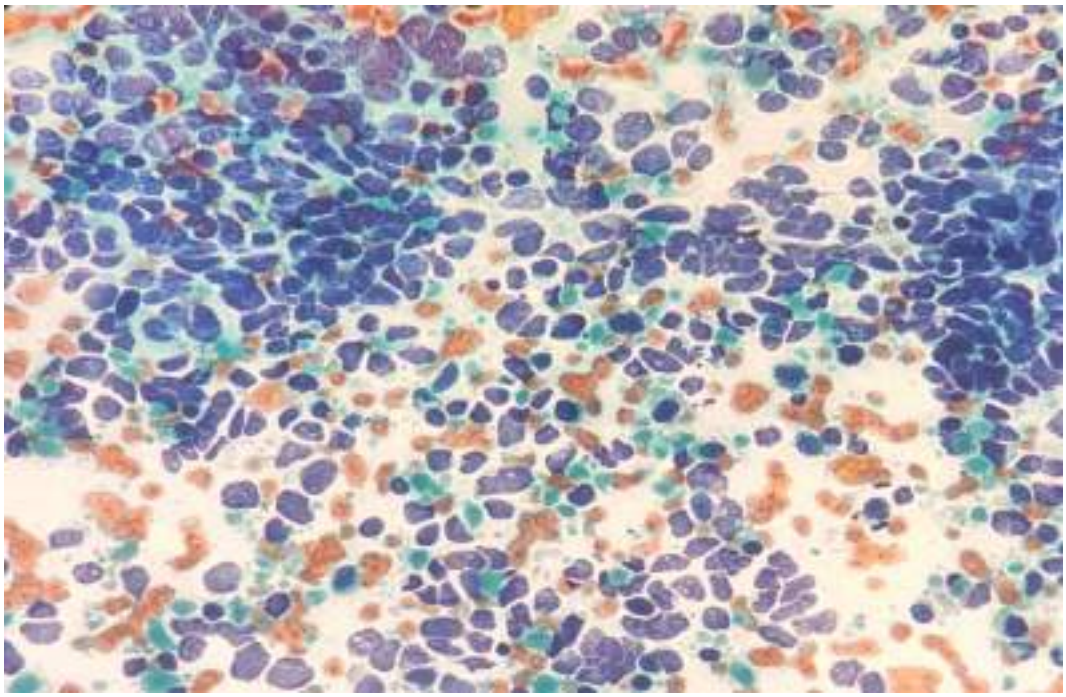

Figure 19: **Small cell carcinoma-** Cytological smear are cellular and show small to medium sized cells with irregular nuclei, finely granular chromatin with scant cytoplasm. Nuclear molding and streaking seen (PAP,400x)

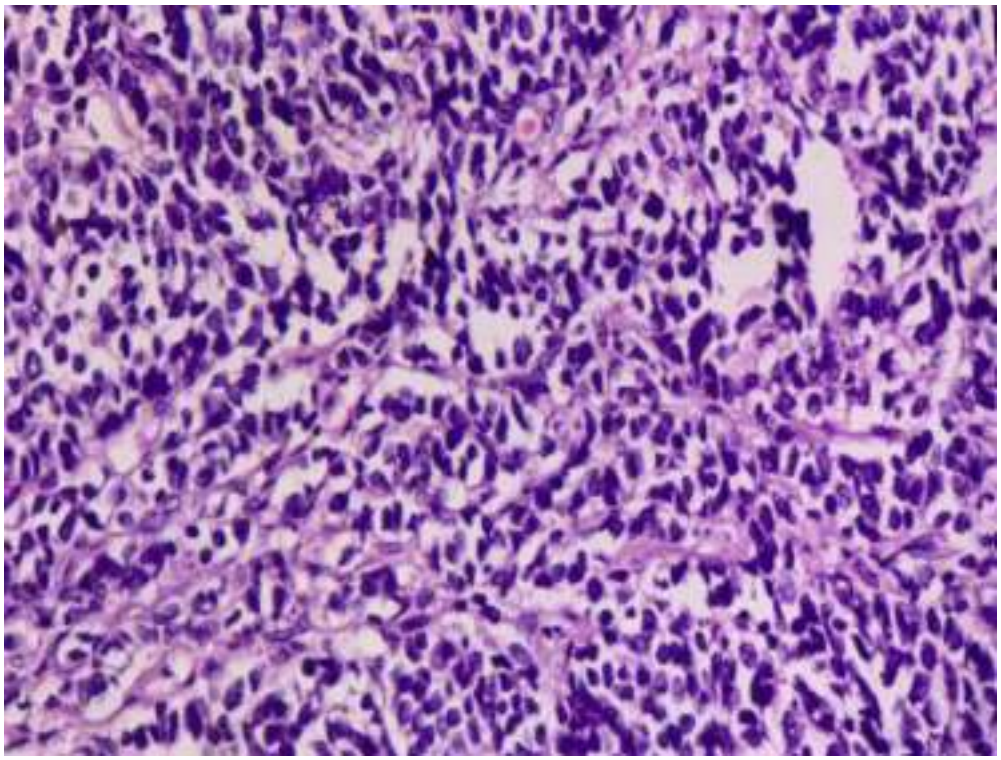

Figure 20 – **Small cell carcinoma-** Histological section shows sheeting pattern of tumor cells with hyperchromatic nuclei and scant amount of cytoplasm (H&E, 400X)

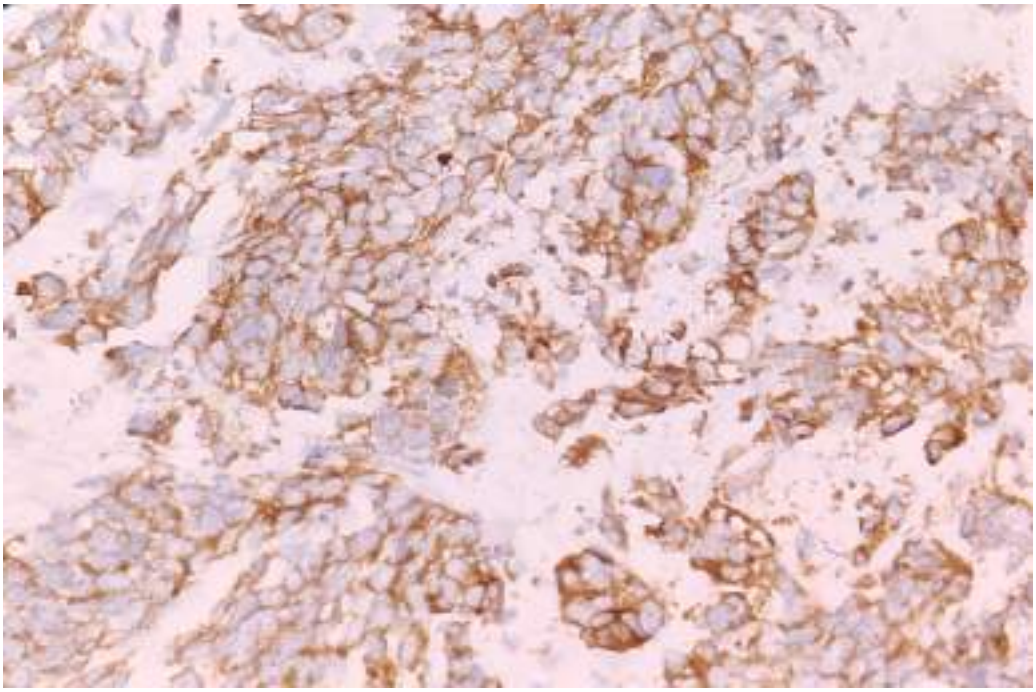

Figure 21: **Small cell carcinoma-** Cells showing diffuse cytoplasmic immunoreactivity for synaptophysin (IHC, 400x**)**

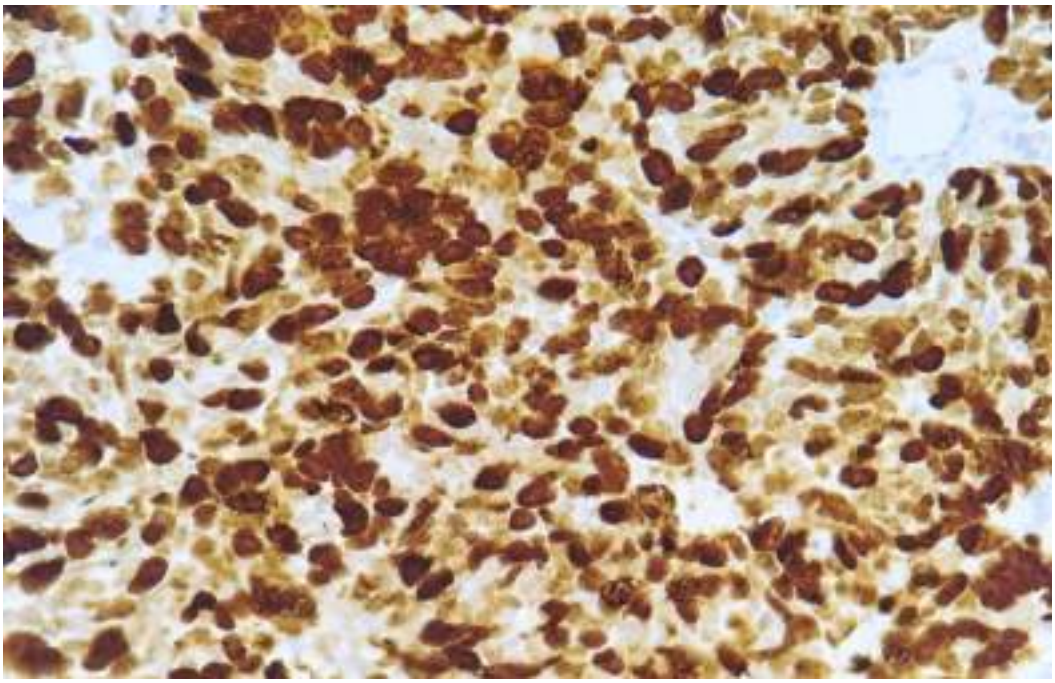

Figure 22: **Small cell carcinoma-** Ki-67 proliferation index 99% (IHC,400x)

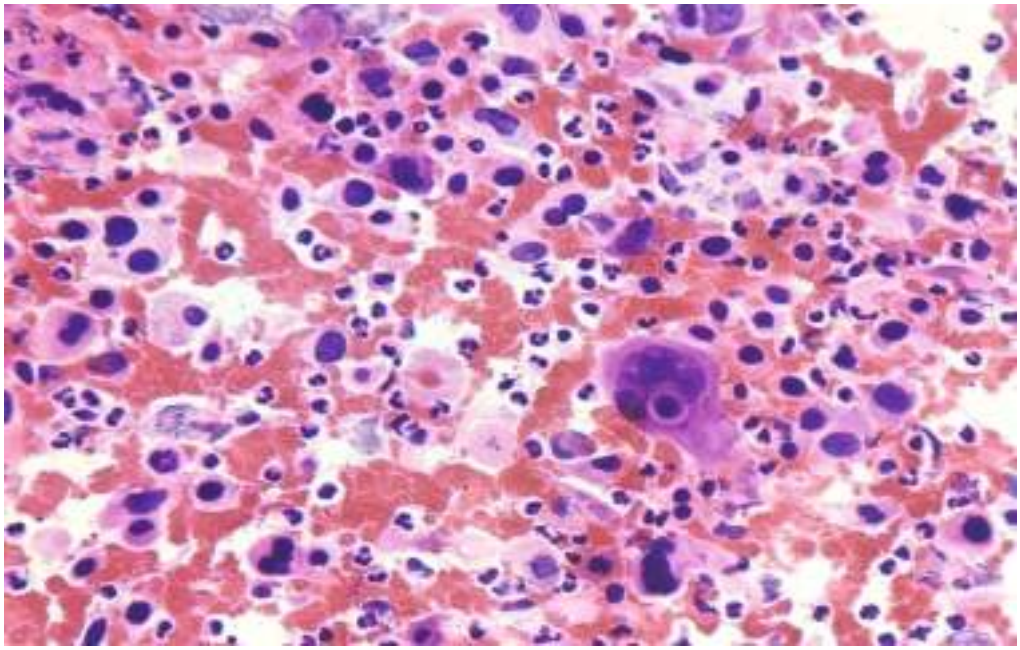

Figure 23: **Metastatic squamous cell carcinoma-Mediastinal Lymph node-** Cytological smear shows atypical cells with variable hyperchromasia, abundant eosinophilic cytoplasm with individual cell keratinization. (H&E,400X)

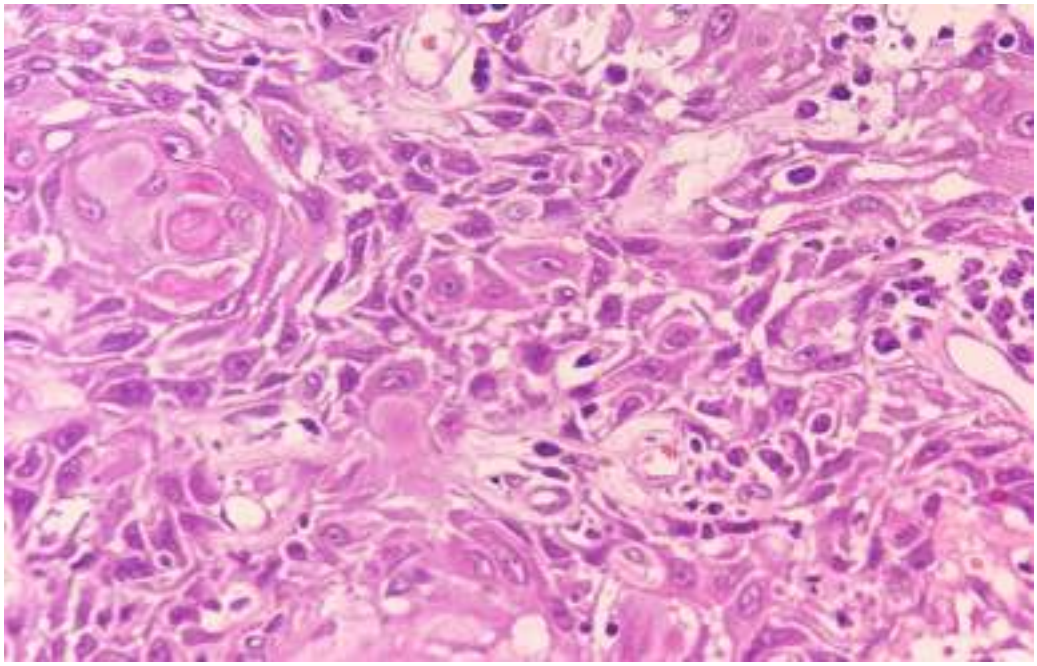

Figure 24: **Metastatic squamous cell carcinoma- Mediastinal Lymphnode** Histological section shows pleomorphic polygonal cells with vesicular nuclei, hyperchromatic nuclei and abundant eosinophilic cytoplasm along with individual cell keratinization and keratin perl;s. (H&E,400x)

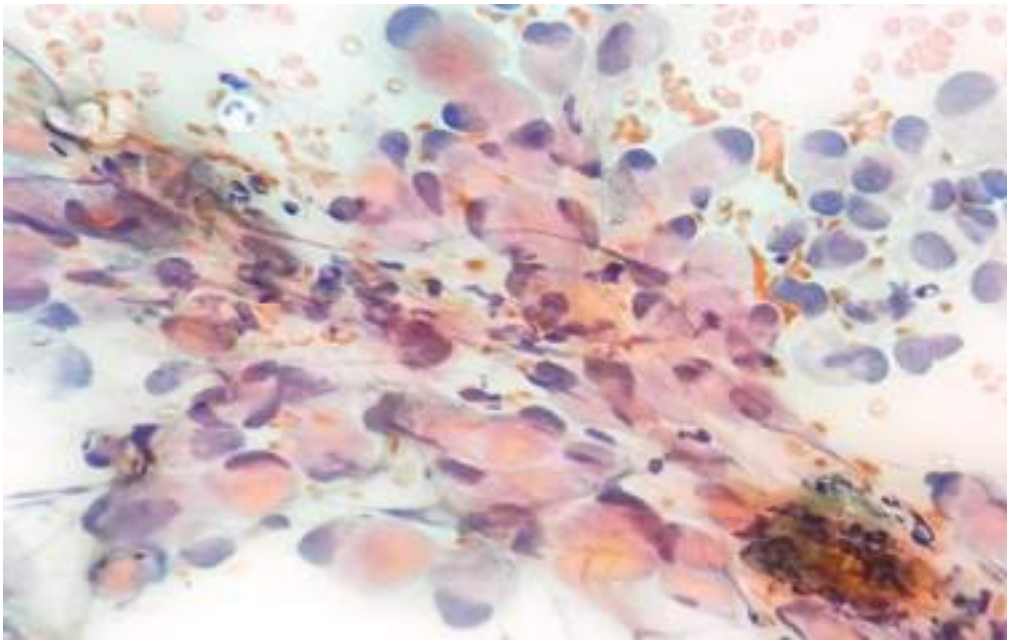

Figure 25: **Schwannian rich neuroblastic tumor-** Cytology smears shows singly scattered ganglion cells having eccentric nucleus with abundant fine eosinophilic cytoplasm along with schwannian stroma (PAP, 100X)

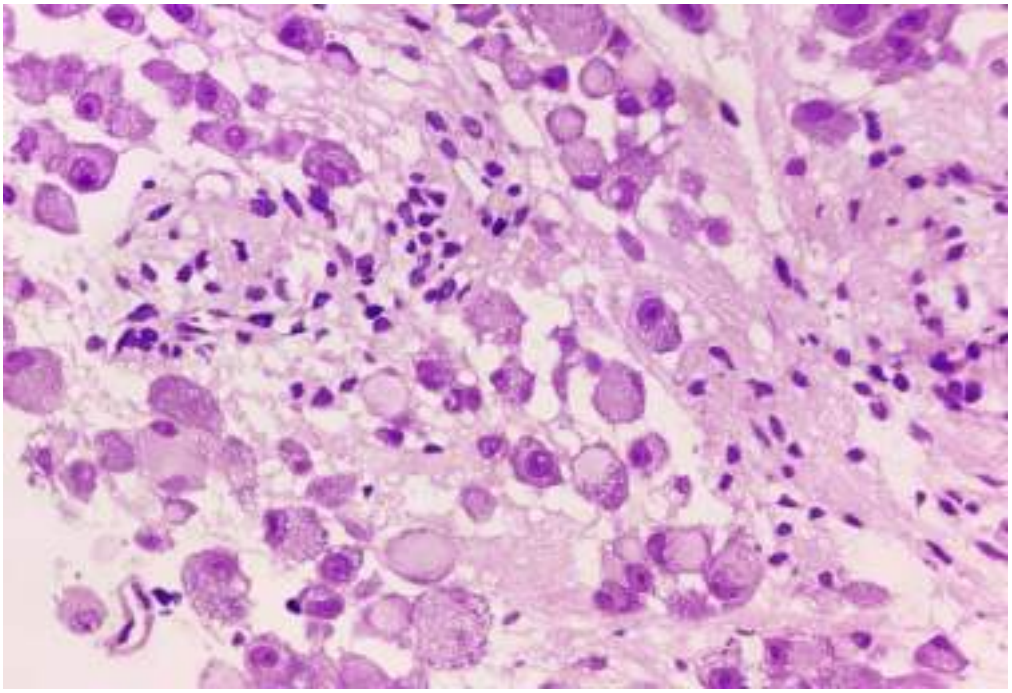

Figure 26: **Schwannian rich neuroblastic tumor-** Histology section shows presence of schwaninan stroma with many ganglion cells and a tiny cluster of neuroblasts. (H&E, 100X)

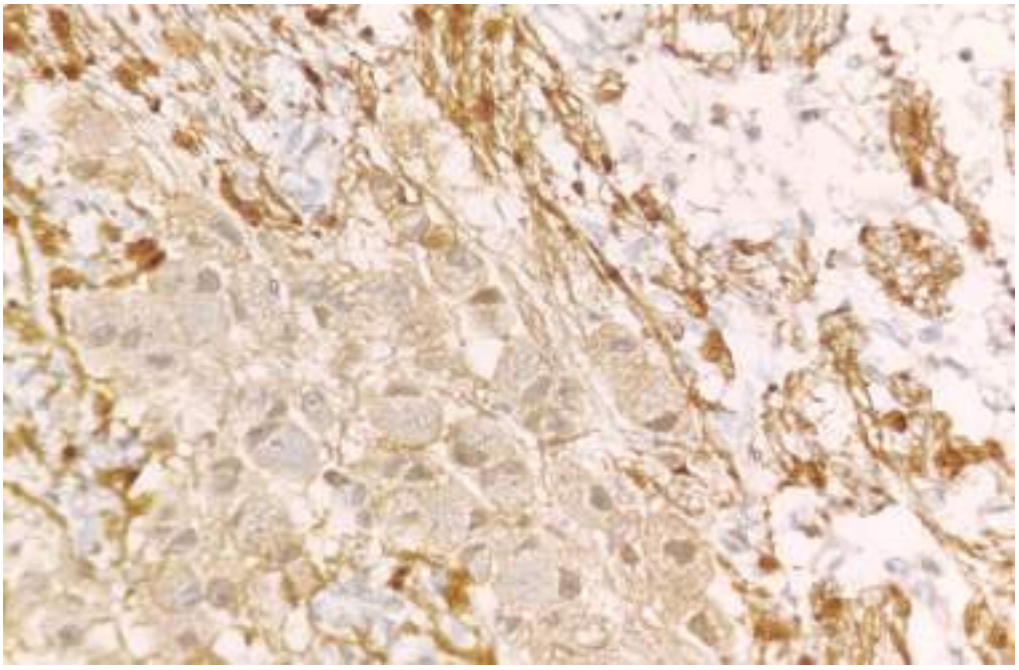

Figure 27**: Schwannian rich neuroblastic tumor-** Cells showing diffuse positivity of S100 in schwannian stroma (IHC, 400x)

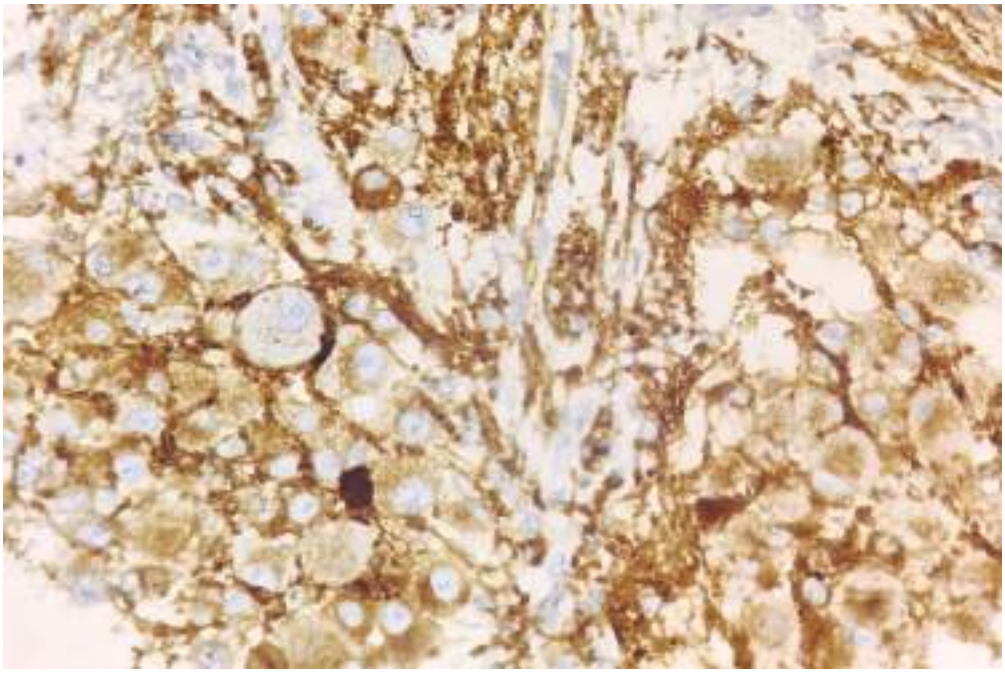

Figure 28**: Schwannian rich neuroblastic tumor-** Cells showing diffuse cytoplasmic immunoreactivity of Synaptophysin in ganglion cells and schwannian stroma (IHC, 400x)

| SR. NO | MRD NO | NAME | CYTOPATH NO | Age | SEX | DURATION | SYMPTOMS | | | | | | PAST HISTORY | RADIOLOGICAL FINDINGS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | FEVER | COUGH | DYSPNEA | CHEST PAIN | HEMOPTYSIS | LOW/LOA | | |
| 1 | 857898 | BB | 2019-1965 | 25 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY-?INFECTIVE ?INFLAMMATORY |
| 2 | 860894 | GS | 2019-1975 | 30 | M | | - | - | - | - | - | - | - | LOBULATED ANTERIOR MEDIASTINAL MASS ?INVASIVE THYMOMA ? LYMPHOMA |
| 3 | 668121 | TR | 2019-2018 | 65 | M | 15YEARS | PRESENT | - | PRESENT | PRESENT | - | PRESENT | DM +; HTN+ | RENAL PARENCHYMAL CHANGES GRADE I |
| 4 | 867362 | AS | 2019-2030 | 25 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY-POSSIBILTY OF TUBERCULOSIS |
| 5 | 126906 | RS | 2016-1101 | 17 | M | | | | | | | | | ANTERIOR MEDIASTINAL MASS LIKELY LYMPHOMA |
| 6 | 136808 | NS | 2016-1289 | 53 | F | | | | | | | | | MEDIASTINAL LYMPHADENOPATHY LIKELY TB |
| 7 | 96997 | CL | 2016-1301 | 55 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | PRESENT | CHRONIC SMOKER | MALIGNANT MASS LESION IN IN LEFT LUNG WITH MEDIASTINAL INFILTRATION |
| 8 | 130202 | S | 2016-1529 | 40 | F | 6 MONTHS | PRESENT | PRESENT | PRESENT | - | - | - | K/C/O TB ON ATT -6MONTHS | NECROTIC MEDIASTINAL LYMPHADENOPATHY |
| 9 | 69622 | GS | 2016-1557 | 54 | M | 1 MONTH | - | PRESENT | PRESENT | - | - | - | k/C/O BRONCHIECTASIS | HETEROGENOUSLY ENHANCING LESION WITH FOCIOF CALCIFIATION?CA LUNG |
| 10 | 13593 | KK | 2016-1586 | 41 | F | 45 DAYS | - | - | PRESENT | - | - | - | - | ANTERIOR MEDIASTINAL MASS -LYMPHOMA/ THYMOMA |
| 11 | 178785 | RK | 2017-126 | 60 | M | - | - | - | - | - | - | - | - | ANTERIOR MEDIASTINAL MASS SUGGESTIVE OF MLIGNANCY |
| 12 | 148457 | SV | 2017-59 | 60 | F | | | | | | | | | |
| 13 | 177997 | MR | 2017-42 | 64 | M | 4 months | - | PRESENT | - | - | - | - | K/C/O TB ON ATT -6MONTHS | LARGE LOBULATED MEDIASTINAL MASS WITH EXTENSIVE MEDIASTINAL LYMPHADENOPATHY ?LYMPHOMA |
| 14 | 175143 | HS | 2017-07 | 26 | M | 6 months | - | - | PRESENT | - | - | PRESENT | SMOKER | ANTERIOR MEDIASTINAL LESION ?GERM CELL TUMOR/ ATYPICAL LYMPHOMATUS MASS |
| 15 | 174261 | RK | 2017-04 | 46 | M | 10 MONTHS | - | PRESENT | - | - | - | PRESENT | - | SUPERIOR MEDIASTINAL MASS ?NAURE/THYMOMA |
| 16 | 195334 | S | 2017-180 | 41 | F | 3 MONTHS | PRESENT | PRESENT | - | - | - | - | - | MEDIASTINAL AND HILAR LYMPHADENOPATHY ?TB/SARCOIDOSIS |
| 18 | 208711 | BD | 2017-293 | 70 | F | 1 YEAR | PRESENT | PRESENT | PRESENT | - | - | - | HTN+ | MEDIASTINAL LYMPHADENOPATHY?SARCOIDOSIS |
| 19 | 222314 | AR | 2017-389 | 74 | M | 3 MONTHS | - | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY ?TB/SARCOIDOSIS/LYMPHOMA |
| 20 | 228537 | AS | 2017-418 | 31 | M | 1 MONTH | PRESENT | PRESENT | - | PRESENT | - | PRESENT | - | MASS LESION IN ANTERIOR MEDIASTINUM ?NEOPLASTIC/INFECTIOUS |
| 21 | 252088 | M | 2017-624 | 52 | M | 3 MONTHS | - | PRESENT | PRESENT | PRESENT | - | PRESENT | K/C/O TB ON ATT | POSTERIOR MEDIASTINAL MASS/?ENLARGED LYMPH NODE |
| 22 | 239467 | RKM | 2017-612 | 81 | M | - | - | - | - | - | - | - | - | - |
| 23 | 241494 | RR | 2017-579 | 42 | F | 1 MONTH | PRESENT | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPTHY ?SARCOIDOSIS/KOCH'S |
| 24 | 244749 | KD | 2017-555 | 60 | F | - | - | - | - | - | - | - | DM- 1 YEAR | FEW DISCRETE MEDIASTINAL NODES SEEN ?TB |
| 25 | 244716 | SS | 2017-553 | 47 | M | 15 DAYS | - | - | - | PRESENT | - | - | DM-=9 YEARS | MEDIASTINAL LYMPHADENOPATHY WITH NECROTIC AREAS ?TB |
| 26 | 355273 | CD | 2018-49 | 65 | M | 2 MONTHS | - | PRESENT | PRESENT | - | - | PRESENT | OLD PULMONARY KOCK'S, COPD, CHRONIC SMOKER | NECROTIC MEDIASTINAL LYMPH NODES ?REACTIVATION OF TB |
| 27 | 441384 | GC | 2018-245 | 65 | M | 1 MONTH | PRESENT | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY |
| 28 | 473300 | JK | 18-584 | 59 | F | - | - | - | - | - | - | - | - | SUPERIOR MEDIASTINAL MASS |
| 29 | 479177 | AR | 18-614 | 35 | F | 6 MONTHS | PRESENT | PRESENT | PRESENT | - | - | PRESENT | K/C/O TB ON ATT | LEFT PLEURAL EFFUSION WITH CONSOLIDATION LEFT LUNG |
| 30 | 482870 | NPK | 18-654 | 54 | F | 2 YEARS | - | - | PRESENT | PRESENT | - | PRESENT | - | HETEROGENOUSLY ENHANCING ANTERIOR MEDIASTINAL MASS ?THYMOMA ?LYMPHOMA |
| 31 | 494406 | AJ | 18-751 | 26 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY |
| 32 | 493855 | RK | 18-799 | 59 | M | 6 MONTHS | - | - | - | - | - | PRESENT | DM=3 MONTHS, K/C/O CHRONIC PANCREATITIS | RIGHT PARATRACHEAL, PRETRACHEAL, SUBCARINAL , PRECARINAL LYMPHADENOPATHY |

| SR. NO | MRD NO | NAME | CYTOPATH NO | Age | SEX | DURATION | SYMPTOMS | | | | | | PAST HISTORY | RADIOLOGICAL FINDINGS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | FEVER | COUGH | DYSPNEA | CHEST PAIN | HEMOPTYSIS | LOW/LOA | | |
| 33 | 42186 | KA | 18-811 | 21 | M | 1 MONTH | PRESENT | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY |
| 34 | 340870 | JS | 18-1040 | 65 | M | | | | | | | | | |
| 35 | 533700 | JS | 18-1125 | 29 | M | | | | | | | | | |
| 36 | 392224 | N | 18-1253 | 27 | F | 1 MONTH | PRESENT | - | - | - | - | PRESENT | K/C/O TB ON ATT FOR 9 MONTHS | ANTERIOR MEDIASTINAL MASS ? PRIMARY THYMIC NEOPLASM ?LYMPHOMA |
| 37 | 557954 | RKK | 18-1368 | 65 | M | 2 MONTHS | - | PRESENT | - | - | - | PRESENT | ALCOHALIC, SMOKER AND K/C/O TB AND CA PANCREAS | MASS HEAD OF PANCREAS WITH MEDIASTINAL LYMPHADENOPATHY LIKELY METASTATIC |
| 38 | 532384 | AK | 18-1387 | 24 | F | 3 MONTHS | PRESENT | - | - | - | - | - | ON ATT SINCE 2 MONTHS | PERIPORTAL LYMPHADENOPATHY ?TB ? SARCOIDOSIS ? OTHERS |
| 39 | 571828 | RC | 18-1480 | 59 | M | 2 MONTHS | PRESENT | - | - | - | - | - | CHRONIC SMOKER X20YEARS | NECROTIC MASS IN ANTERIOR MEDIASTINUM |
| 40 | 562838 | KS | 18-1481 | 60 | M | 12 DAYS | - | - | - | PRESENT | - | - | DM, HTN X7YEARS | LARGE HETEROGENOUS MASS IN SUPERIOR MEDIASTINUM 5X4 CM |
| 41 | 579053 | NK | 18-1551 | 38 | M | - | - | - | - | - | - | - | - | MEDIASTINUM LYMPHADENOPATHY 3.8X3mm ?SARCOIDOSIS VS TB ?LYMPHOMA |
| 42 | 580775 | SK | 18-1582 | 56 | F | 2 MONTHS | PRESENT | - | - | - | - | - | - | HETEROGENOUSLY ENHANCING LESION IN AP WINDOW ? LYMPH NODE METASTASIS |
| 43 | 588193 | TK | 18-1674 | 24 | F | 3 DAYS | - | - | - | PRESENT | - | - | - | WELL DEFINED ENHANCING MASS LESION IN ANTERIOR MEDIASTINUM |
| 44 | 599525 | ML | 18-1750 | 60 | M | 2 MONTHS | PRESENT | - | - | - | - | - | DMX 15 YEARS | NECROTIC LEFT HILAR MASS WITH MEDIASTINAL LYMPHADENOPATHY LIKELY MALIGNANT |
| 45 | 628798 | NP | 18-1983 | 33 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | MULTIPLE NON NECROTIC LYMPH NODES IN MEDIASTINUM, SUBCARINAL ?SARCOIDOSIS |
| 46 | 277593 | RG | 18-1984 | 27 | M | 2 MONTHS | PRESENT | - | - | - | - | PRESENT | KNEE AND ANKLE PAIN | BILATERAL MEDIASTINUM LYMPH NODES ?SARCOIDOSIS ?TB |
| 47 | | PK | 17-661 | 18 | F | 5 DAYS | - | PRESENT | - | - | - | - | - | MASSIVE BILATERAL MEDIASTINAL LYMPHADENOPATHY ?TB?LYMPHOMA 4.3X4.8cm |
| 48 | 178932 | PS | 17-755 | 65 | M | 5 MONTHS | - | - | - | - | - | PRESENT | K/C/O CA ESOPHAGUS | HYPOECHOIC LESION SEEN IN CLOSE APPROXIMITY TO CARDIAC CHAMBER |
| 49 | 279863 | AK | 17-862 | 52 | M | 2 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | - | MIDDLE MEDIASTINAL MASS ?LYMPHOMA 78X59mm |
| 50 | 273169 | DK | 17-894 | 65 | F | - | - | - | - | - | - | - | - | MULTIPLE MEDIASTINAL LYMPH NODES IN SUBCARINAL AREAS |
| 51 | 294538 | SC | 17-1004 | 34 | M | 1 MONTH | - | PRESENT | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY ?TB/SARCOIDOSIS |
| 52 | 294538 | SC | 17-1015 | 34 | M | 1 MONTH | - | PRESENT | - | - | - | - | - | MEDIASTINAL LYMHPHADENOPATHY ?TB |
| 53 | 296888 | MK | 17-1050 | 45 | F | 10 DAYS | - | PRESENT | PRESENT | PRESENT | - | - | K/C/O BRONCHIAL ASTHMA X 18YEARS | LARGE MASS 5X6mm IN MIDDLE MEDIASTINUM ?LYMPHOMA |
| 54 | 266710 | D | 17-1127 | 40 | F | 1 YEAR | PRESENT | PRESENT | - | - | - | - | K/C/O EXTRAPULMONARY TB ON ATT | MLTIPLE TINY NODULES IN BILATERAL LUNGS WITH MEDIASTINAL LYMPHADENOPATHY 3.7X3.6cm ?INFECTIVE |
| 55 | 272031 | BK | 17-1140 | 75 | F | - | - | - | - | - | - | - | - | ENLARGED MEDIASTINAL LYMPH NODES ?MALIGNANT |
| 56 | 312272 | KR | 17-1165 | 55 | F | 6 MONTHS | - | PRESENT | - | - | - | - | - | LARGE LOBULATED MASS IN ANTERIOR MEDIASTINUM 9.4X7.5 cm?THYMOMA |
| 57 | 317877 | HK | 17-1199 | 21 | F | 2 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | - | ANTERIOR MEDIASTINAL MASS ?THYMOMA/LYMPHOMA |
| 58 | 322582 | SS | 17-1241 | 18 | M | 6 DAYS | PRESENT | - | - | - | - | - | K/C/O INFECTIVE ENDOCARDITIS | HOMOGENOUS MASS IN MIDDLE AND POSTERIOR MEDIASTINUM WITH LARGE LYMPH NODES 4X3cm ?TB |
| 59 | 340870 | JS | 17-1424 | 65 | M | 3 WEEKS | PRESENT | PRESENT | - | - | - | PRESENT | - | MULTIPLE ENLARGED LYMPH NODES IN PRETRACHEAL AND MEDIASTINUM 15mm ?TB?SARCOIDOSIS |
| 60 | 344271 | BL | 17-1428 | 71 | M | 1 month | PRESENT | - | - | - | - | PRESENT | - | IRREGULRALY MARGINATED MASS 9.4X5 cm IN ANTERIOR MEDIASTINUM ?MITOTIC |
| 61 | 382559 | SK | 17-1755 | 45 | F | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | MEDIASTINAL AND B/L HILAR LYMPHADENOPATHY |

| SR. NO | MRD NO | NAME | CYTOPATH NO | Age | SEX | DURATION | SYMPTOMS | | | | | | PAST HISTORY | RADIOLOGICAL FINDINGS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | FEVER | COUGH | DYSPNEA | CHEST PAIN | HEMOPTYSIS | LOW/LOA | | |
| 62 | 386950 | HS | 17-1750 | 59 | M | 1 MONTH | PRESENT | PRESENT | - | PRESENT | - | PRESENT | - | MIDDLE MEDIASTINAL LYMPHADENOPATHY ?INFECTIVE/INFLAMMATORY/NEOPLASTIC |
| 63 | 389728 | KK | 17-1778 | 16 | F | 1 MONTH | - | - | PRESENT | PRESENT | - | - | - | HETEROGENOUS MASS LESION IN ANTERIOR MEDIASTINUM ?METASTASIS |
| 64 | 397810 | RS | 17-1865 | 22 | M | 1 MONTH | PRESENT | PRESENT | - | - | - | - | - | ANTERIOR MEDIASTINAL MASS ?LN 2X3cm ?infective |
| 65 | 408552 | AA | 17-1952 | 43 | F | 1 MONTH | - | - | - | - | - | PRESENT | - | MASS LESION IN ANTERIOR MEDIASTINUM S/O THYMOMA/ GERM CELL NEOPLASM |
| 66 | 411752 | HS | 17-1970 | 67 | M | 6 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | COPD, SMOKER, TB ON ATT | ANTERIOR MEDIASTINAL MASS ?LYMPHOMA/TB |
| 67 | 686079 | JS | 19-345 | 74 | M | 3MONTHS | - | - | PRESENT | - | - | PRESENT | K/C/O PULM. KOCHS ON ATT | ANTERIOR MEDIASTINAL MASS |
| 68 | 692209 | R | 19-363 | 45 | F | 2 DAYS | - | - | PRESENT | - | - | - | HTN+ | MEDIASTINAL LYMPHADENOPATHY-?SARCOIDOSIS |
| 69 | 624858 | JK | 19-414 | 57 | F | 8MONTHS | - | PRESENT | - | - | - | - | K/C/O ILD | MEDIASTINAL LYMPHADENOPATHY? INFLAMMATORY |
| 70 | 698031 | LS | 19-429 | 26 | M | | - | - | - | - | - | - | - | MEDIASTINAL LESION ? CARCINOMA? BENIGN |
| 71 | 701771 | RS | 19-446 | 66 | M | 6MONTHS | - | PRESENT | PRESENT | PRESENT | - | PRESENT | SMOKER | ANTERIOR MEDIASTINAL LESION LIKELY MALIGNANT |
| 72 | 704541 | LKB | 19-473 | 32 | F | 2 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | - | MEDIASTINAL LYMPH NODAL MASS? INFECTIVE/METASTATIC |
| 73 | 704416 | BS | 19-535 | 59 | M | | - | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY ?INFECTIVE/INFLAMMATORY |
| 74 | 723020 | SK | 19-662 | 38 | F | 3MONTHS | PRESENT | PRESENT | PRESENT | PRESENT | - | - | H/O TB CONTACT | ANTERIOR MEDIASTINAL MASS? LYMPHOMA/GCT |
| 75 | 672472 | GK | 19-713 | 60 | F | 7YEARS | - | - | - | - | - | PRESENT | - | MEDIASTINAL LYMPHADENOPATHY ?INFECTIVE/INFLAMMATORY |
| 76 | 37170 | SS | 19-812 | 67 | F | 3 YEARS | - | - | - | - | - | PRESENT | K/C/O NHL ON CHEMOTHERAPHY | MEDIASTINAL LYMPHADENOPATHY? NHL/TB |
| 77 | 672472 | GK | 19-857 | 60 | F | 1 MONTH | PRESENT | - | - | - | - | - | - | MEDIASTINAL LYMPHADENOPATHY? INFECTIVE/INFLAMMATORY |
| 78 | 746433 | SK | 19-906 | 26 | F | 1 MONTH | - | PRESENT | - | - | - | - | - | LEFT HILAR CASEATING LYMPHADENOPATHY |
| 79 | 682824 | HS | 19-918 | 39 | M | 2 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | - | NECROTIC MEDIASTINAL LYMPHADENOPATHY S/O TUBERCULAR ETIOLOGY |
| 80 | 751139 | SK | 19-1070 | 32 | F | 3 MONTHS | - | - | - | - | - | - | - | LOBULATED ANTERIOR MASS LESION ? LYMPHOMA |
| 81 | 761228 | NL | 19-1097 | 60 | M | 7 DAYS | - | PRESENT | - | - | - | - | - | ANTERIOR MEDIASTINAL SOFT TISSUE LESION-MALIGNANT |
| 82 | 782757 | D | 19-1274 | 60 | M | 2 MONTHS | - | PRESENT | - | - | - | PRESENT | SMOKER X15 YEARS, COPD, DM | MEDIASTINAL AND HILAR LYMPHADENOPATHY-POSSIBLY NEOPLASTIC |
| 83 | 796867 | AK | 19-1439 | 37 | M | 3 MONTHS | PRESENT | PRESENT | - | - | - | PRESENT | - | MEDIASTINAL LYMPH NODE-POSSIBLY TB |
| 84 | 813248 | SM | 19-1573 | 54 | F | 1 MONTH | PRESENT | - | - | - | - | - | - | MEDIASTINAL LYMPH NODE-?SARCOIDOSIS/KOCHS |
| 85 | 835928 | PK | 19-1793 | 58 | F | - | - | - | - | - | - | - | K/C/O CA ENDOMETRIUM | MEDIASTINAL LYMPHADENOPATHY?INFECTIVE/INFLAMMATORY |
| 86 | 888131 | BK | 20-128 | 76 | M | 2 MONTHS | PRESENT | - | PRESENT | - | - | PRESENT | - | MIDDLE & POSTERIOR MEDIASTINUM MASS LESION-MALIGNANT |
| 87 | 899094 | HK | 20-280 | 54 | F | | | | | | | | | NECROTIC MEDIASTINAL MASS WITH EXTENSION INTO RT LUNG-MALIGNANCY |
| 88 | 191371 | MR | 20-310 | 38 | F | 1 MONTH | PRESENT | - | - | - | - | - | PATIENT IS ON ATT | MEDIASTINAL LYMPHADENOPATHY |
| 89 | 912347 | BK | 20-356 | 58 | F | 5 MONTHS | - | - | PRESENT | - | - | PRESENT | K/C/O CA ESOPHAGUS | |
| 90 | 945549 | SS | 20-800 | 55 | M | 20 DAYS | PRESENT | - | - | - | - | - | - | ANTERIOR MEDIASTINUM MASS WITH LIVER SOL'S-P/O LYMPHOPROLIFERATIVE DISORDER |
| 91 | 963973 | SS | 20-919 | 29 | M | 1 MONTH | - | - | - | PRESENT | - | - | LARGE LEFT ATRIUM CLOT | MIDDLE MEDIASTINUM SOFT TISSUE MASS-P/O GCT/HIGH GRADE LYMPHOMA |
| 92 | 964071 | RK | 20-916 | 30 | F | 1 MONTH | - | PRESENT | - | - | - | - | - | MID PARA AORTIC CONSOLIDATION |
| 93 | 1006973 | HS | | 49 | M | 2 MONTHS | - | - | - | - | - | PRESENT | OLD CASE OF METASTATIC NEUROENDOCRINE TUMOR | ANTERIOR MEDIASTINAL MASS ?PARAGANGLIOMA |

| SR. NO | MRD NO | NAME | CYTOPATH NO | Age | SEX | DURATION | SYMPTOMS | | | | | | PAST HISTORY | RADIOLOGICAL FINDINGS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | FEVER | COUGH | DYSPNEA | CHEST PAIN | HEMOPTYSIS | LOW/LOA | | |
| 94 | 992720 | SA | 20-1154 | 2 | M | 2 MONTH | PRESENT | PRESENT | - | - | - | PRESENT | | LARGE HETEROGENOUS MASS IN POSTERIOR MEDIASTINUM 16.5X18cm ?PNET/NEUROBLASTOMA |
| 95 | 1009083 | GS | 21-31 | 32 | M | 6 MONTHS | PRESENT | PRESENT | PRESENT | - | - | - | - | ANTERIOR MEDIASTINUM MASS LESION 11X8X18 cm |
| 96 | 1023325 | RS | 21-159 | 38 | F | 2 DAYS | - | PRESENT | PRESENT | PRESENT | - | - | - | POSTERIOR MEDIASTINAL MASS 2.5X2CM ?LYMPHOMA |
| 97 | 631597 | SS | 21-201 | 42 | M | 4 DAYS | - | - | PRESENT | PRESENT | - | PRESENT | HTN, RENAL TRANSPLANT IN 2019 | ANTERIOR MEDIASTINAL MASS |
| 98 | 1027220 | AG | 21-213 | 61 | M | 15 DAYS | - | - | PRESENT | - | - | - | DM,HTN X12 YEARS | ANTERIOR MEDIASTINUM MASS WITH BULKY LYMPH NODES 4.8X5CM ?LYMPHOMA |
| 99 | 104058 | RK | 21-330 | 66 | M | 1 MONTH | PRESENT | - | - | PRESENT | - | PRESENT | COVID IN OCT 2019 | ANTERIOR MEDIASTINUM MASS POSSIBLY MALIGNANT ?CLL |
| 100 | 1087436 | SS | 21-545 | 34 | M | 2 MONTHS | PRESENT | - | - | - | - | PRESENT | - | MULTIPLE ANTERIOR MEDIASTINAL LN , NON-NECROTIC 2X2.8CM ?TB/SARCOIDOSIS/LYMPHOMA |
| 101 | 1112650 | HSS | 21-615 | | M | 2 MONTHS | - | - | - | - | - | PRESENT | K/C/O MEDIASTINAL GCT | ANTERIOR MEDIASTINAL MASS |
| 101 | 1103669 | LS | 21-633 | 73 | M | 2 MONTHS | PRESENT | PRESENT | PRESENT | - | - | PRESENT | - | ANTERIOR MEDIASTINAL MASS |
| 102 | 1121064 | GS | 21-679 | 23 | M | 1 MONTH | - | PRESENT | PRESENT | PRESENT | - | - | K/C/O T-LYMPHOBLASTIC LYMPHOMA | ANTERIOR MEDIASTINUM MASS 4X5CM |

| SR. NO | MRD NO | BIOCHEMISTRY | Mode of FNAC | SITE | CELLULARITY | ARCHITECTURAL PATTERN | TUMOR CELLS | GRANULOMAS | NECROSIS |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 857898 | Ca2+=10; ACE=130 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 2 | 860894 | ESR=62; LDH=764 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | CLUSTERS & SHEETS | PRESENT | - | - |
| 3 | 668121 | ESR=120; Ca2+=9.1 | USG GUIDED | MIDDLE MEDIASTINAL MASS | | - | PRESENT | - | - |
| 4 | 867362 | - | EUS GUIDED | ANTERIOR MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 5 | 126906 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | - | PRESENT | - | - |
| 6 | 136808 | ESR=110 | USG GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 7 | 96997 | - | CT GUIDED | SUPERIOR MEDIASTINAL MASS | HIGHLYCELLULAR | - | PRESENT | - | - |
| 8 | 130202 | - | CT GUIDED | ANTERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | - | - | PRESENT | - |
| 9 | 69622 | - | CT GUIDED | POSTERIOR MEDIASTINAL LN | BLOOD ONLY | - | - | - | - |
| 10 | 13593 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | - | PRESENT | - | - |
| 11 | 178785 | - | | ANTERIOR MEDIASTINAL MASS | | CLUSTERS AND PAPILLARY FRAGMENTS | PRESENT | - | - |
| 12 | 148457 | | CT GUIDED | MIDDLE MEDIASTINAL MASS | PAUCICELLULAR | - | - | - | - |
| 13 | 177997 | ESR=24 | USG GUIDED | SUPERIOR MEDIASTINAL MASS | | TINY CLUSTERS &SINGELY DISSOCIATED | PRESENT | - | - |
| 14 | 175143 | Ca2+=10.6 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | SINGELY SCATTERED | PRESENT | - | - |
| 15 | 174261 | - | USG GUIDED | SUPERIOR MEDIASTINAL MASS | CELLULAR | COHESIVE CLUSTERS | PRESENT | - | - |
| 16 | 195334 | ACE=38 | EUS GUIDED | MIDDLE MEDIASTINAL LN | CELLULAR | - | - | PRESENT | - |
| 18 | 208711 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | CLUSTERS & SINGELY SCATTERED | - | - | - |
| 19 | 222314 | ESR=28 | EUS GUIDED | MIDDLE MEDIASTINAL LN | SCANTILY CELLULAR | - | - | - | - |
| 20 | 228537 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | FEW CLUSTERS | - | - | - |
| 21 | 252088 | ESR=75 | CT GUIDED | POSTERIOR MEDIASTINAL MASS | - | SCATTERED | PRESENT | - | PRESENT |
| 22 | 239467 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | - | - | - | - |
| 23 | 241494 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | - | - | PRESENT | - |
| 24 | 244749 | ESR=65 | EUS GUIDED | MIDDLE MEDIASTINAL LN | DEGENERATED SMEAR | SINGELY DISPERSED | - | - | - |
| 25 | 244716 | HIV=NR | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | - | - | PRESENT | PRESENT |
| 26 | 355273 | ESR=119, Ca2+=8.9 | USG GUIDED | ANTERIOR MEDIASTINAL LN | CELLULAR | PAPILLAROID & SINGELY SCATTERED | PRESENT | - | PRESENT |
| 27 | 441384 | ESR=10 | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | - | - | PRESENT | PRESENT |
| 28 | 473300 | ESR=23, LDH=86, ACE=59, Ca2+=8.3, CEA=8.80, CA19-9=0.8 | USG GUIDED | SUPERIOR MEDIASTINAL MASS | | - | - | - | - |
| 29 | 479177 | ESR=70, LDH=199, ACE=44.46, Ca2+=8.5 | USG GUIDED | MIDDLE MEDIASTINAL LN | HEMORRHAGIC | SINGELY SCATTERED | PRESENT | - | - |
| 30 | 482870 | LDH=203, AFP=2.48, B-HCG=2.90 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | - | COHESIVE CLUSTERS | PRESENT | - | - |
| 31 | 494406 | ESR=03, Ca2+=9.8 | EUS GUIDED | MIDDLE MEDIASTINAL LN | HEMORRHAGIC | - | - | PRESENT | - |
| 32 | 493855 | ESR=27, LDH=170, ACE=66.2, Ca2+=9.2 | EUS GUIDED | ANTERIOR MEDIASTINAL MASS | - | - | - | - | - |

| SR. NO | MRD NO | BIOCHEMISTRY | Mode of FNAC | SITE | CELLULARITY | ARCHITECTURAL PATTERN | TUMOR CELLS | GRANULOMAS | NECROSIS |
|---|---|---|---|---|---|---|---|---|---|
| 33 | 42186 | ESR=10, ACE=146, Ca2+=10.1 | USG GUIDED | SUPERIOR MEDIASTINAL LN | - | - | - | PRESENT | - |
| 34 | 340870 | - | EUS GUIDED | ANTERIOR MEDIASTINAL LN | | - | - | - | - |
| 35 | 533700 | AFP=2, B-HCG=0.1, LDH=158 | USG GUIDED | POSTERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | SCATTERED | - | - | - |
| 36 | 392224 | ESR=10, Ca2+=8.5, ACE=20.6 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | - | SINGELY DISSOCIATED & COHESIVE CLUSTERS | - | - | PRESENT |
| 37 | 557954 | HIV=NR | EUS GUIDED | MIDDLE MEDIASTINAL LN | HYPERCELLULAR | - | PRESENT | - | - |
| 38 | 532384 | ESR=69 | EUS GUIDED | SUPERIOR MEDIASTINAL LN | - | - | - | PRESENT | - |
| 39 | 571828 | ESR=25 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | CLUSTERS | PRESENT | - | PRESENT |
| 40 | 562838 | - | USG GUIDED | SUPERIOR MEDIASTINAL MASS | BLOOD | - | - | - | - |
| 41 | 579053 | ESR=27, CA2+=9.1 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 42 | 580775 | - | CT GUIDED | ATERIOR MEDIASTINAL MASS | BLOOD | - | - | - | - |
| 43 | 588193 | - | CT GUIDED | ANTERIOR MEDIASTINAL MASS | PAUCICELLULAR | - | PRESENT | - | - |
| 44 | 599525 | ESR=29, Ca2+=7.6 | CT GUIDED | POSTERIOR MEDIASTINAL MASS | | 3D CLUSTERS & SINGELY SCATTERED | PRESENT | - | - |
| 45 | 628798 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | - | - | PRESENT | - |
| 46 | 277593 | ESR=24, CA2+=9.3, CRP=41.4,S.ACE=68.6 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 47 | | - | USG GUIDED | ANTERIOR MEDIASTINAL LN | - | - | - | PRESENT | - |
| 48 | 178932 | - | USG GUIDED | SUPERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | TINY CLUSTERS & SCATTERED | - | - | - |
| 49 | 279863 | - | CT GUIDED | MIDDLE MEDIASTINAL MASS | CELLULAR | SINGELY SCATTERED & CLUSTERS | PRESENT | - | - |
| 50 | 273169 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | - | - |
| 51 | 294538 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | SCANTILY CELLULAR | SINGELY SCATTERED & CLUMPS | - | - | - |
| 52 | 294538 | - | EUS GUIDED | ANTERIOR MEDIASTINAL LN | | - | - | PRESENT | - |
| 53 | 296888 | - | USG GUIDED | MIDDLE MEDIASTINAL MASS | CELLULAR | COHESIVE CLUSTERS | PRESENT | - | - |
| 54 | 266710 | S.ACE=202 | USG GUIDED | LEFT MEDIASTINAL LN | PAUCICELLULAR | - | - | - | - |
| 55 | 272031 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | SCANTILY CELLULAR | - | - | - | - |
| 56 | 312272 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | BLOOD | - | - | - | - |
| 57 | 317877 | ESR=60, LDH=308 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | - | PRESENT | - | - |
| 58 | 322582 | - | EUS GUIDED | MIDDLE MEDIASTINUM | - | - | - | - | - |
| 59 | 340870 | - | EUS GUIDED | SUPERIOR MEDIASTINAL LN | - | - | - | PRESENT | PRESENT |
| 60 | 344271 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | MODERATELY CELLULAR | CLUSTERS & SINGELY SCATTERED | PRESENT | - | PRESENT |
| 61 | 382559 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | - | - | - | - | - |

| SR. NO | MRD NO | BIOCHEMISTRY | Mode of FNAC | SITE | CELLULARITY | ARCHITECTURAL PATTERN | TUMOR CELLS | GRANULOMAS | NECROSIS |
|---|---|---|---|---|---|---|---|---|---|
| 62 | 386950 | - | USG GUIDED | MIDDLE MEDIASTINAL LYMPH NODES | - | - | - | - | - |
| 63 | 389728 | B-HCG=1.25, AFP=2.37 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | SINGELY SCATTERED | PRESENT | - | PRESENT |
| 64 | 397810 | MONTOUX=PRESENT | USG GUIDED | ANTERIOR MEDIASTINAL MASS | - | - | - | PRESENT | PRESENT |
| 65 | 408552 | LDH=175 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | LOOSELY COHESIVE CLUSTERS & SINGELY DISPERSED | PRESENT | - | - |
| 66 | 411752 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | SINGELY DISSOCIATED | PRESENT | - | - |
| 67 | 686079 | ACE=70 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | - | - | - | - |
| 68 | 692209 | ESR=31 ; Ca2+=9 | USG GUIDED | RIGHT MEDIASTINAL LN | | - | - | PRESENT | - |
| 69 | 624858 | ESR=64; Ca2+=9.1, ACE=54.6 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 70 | 698031 | ESR=03; Ca2+=9.1 | EUS GUIDED | ANTERIOR MEDIASTINAL LESION | SCANTILY CELLULAR | - | - | - | - |
| 71 | 701771 | ESR=69 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | SHEETS & CROWDED CLUSTERS | PRESENT | - | PRESENT |
| 72 | 704541 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | HEMORRHAGIC | - | - | - | - |
| 73 | 704416 | ESR=22; ACE=106; Ca2+=10.2 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 74 | 723020 | LDH=685; CA19.9=9.5; CEA=1.52; AFP=2.10 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | SINGELY SCATTERED | PRESENT | - | - |
| 75 | 672472 | ESR=22;ACE=109; CEA=2.85; CA19.9=26.4;CA125=21.8 | EUS GUIDED | MIDDLE MEDIASTINAL LN | HEMORRHAGIC | - | - | - | - |
| 76 | 37170 | ESR=28; LDH=188;ACE=91 | EUS GUIDED | ANTERIOR MEDIASTINAL LN | | CLUSTERS | - | - | - |
| 77 | 672472 | ESR=25;ACE=109.4;CA19.9=26.4;CEA=2.85;Ca2+=9.7 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | - | - |
| 78 | 746433 | - | USG GUIDED | RIGHT SUPERIOR MEDIASTINAL LN | | - | - | PRESENT | PRESENT |
| 79 | 682824 | - | USG GUIDED | RIGHT SUPERIOR MEDIASTINAL LN | HEMORRHAGIC | - | - | - | - |
| 80 | 751139 | ESR=45;Ca2+=8.9 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | COHESIVE CLUSTERS | - | - | - |
| 81 | 761228 | - | USG GUIDED | ANTERIOR MEDIASTINAL MASS | | SHEETS | PRESENT | - | - |
| 82 | 782757 | - | USG GUIDED | SUPERIOR MEDIASTINAL MASS | | DISPERSED | PRESENT | - | PRESENT |
| 83 | 796867 | ESR=11; ACE=125;Ca2+=9.1 | EUS GUIDED | MIDDLE MEDIASTINAL LN | | - | - | PRESENT | - |
| 84 | 813248 | - | EUS GUIDED | MIDDLE MEDIASTINAL LN | SCANTILY CELLULAR | - | - | - | - |
| 85 | 835928 | Ca2+=8.9 | EUS GUIDED | ANTERIOR MEDIASTINAL LN | | - | - | PRESENT | - |
| 86 | 888131 | ESR=120; LDH=157;Ca2+=12.1 | USG GUIDED | POSTERIOR MEDIASTINAL MASS | | SINGELY SCATTERED & CLUSTERS | PRESENT | - | PRESENT |
| 87 | 899094 | ESR=120;LDH=211;CA19.9=68;AFP=1.09;ADA=41.85;CEA=23.57 | USG GUIDED | SUPERIOR MEDIASTINAL MASS | | - | | | |
| 88 | 191371 | ESR=27;LDH=123; ACE=140 | USG GUIDED | ANTERIOR MEDIASTINAL LN | | - | - | PRESENT | - |
| 89 | 912347 | - | CT GUIDED | POSTERIOR MEDIASTINAL ABSCESS | | SCATTERED | PRESENT | - | PRESENT |
| 90 | 945549 | LDH=324; CEA=2.20;CA19.9=41.45 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | CLUSTERS & SCATTERED | PRESENT | - | - |
| 91 | 963973 | ESR=70;LDH=760; Ca2+=8.5AFP=2.30 | CT GUIDED | MIDDLE MEDIASTINAL MASS | BLOOD | - | - | - | - |
| 92 | 964071 | - | R.P.S | ANTERIOR LYMPH NODE | SCANTILY CELLULAR | | - | PRESENT | - |
| 93 | 1006973 | CA2+=8.4, HIV=NR | CT GUIDED | ANTERIOR MEDIASTINAL MASS | - | SINGELY SCATTERED AND CLUSTERS | PRESENT | - | - |

| SR. NO | MRD NO | BIOCHEMISTRY | Mode of FNAC | SITE | CELLULARITY | ARCHITECTURAL PATTERN | TUMOR CELLS | GRANULOMAS | NECROSIS |
|---|---|---|---|---|---|---|---|---|---|
| 94 | 992720 | - | USG GUIDED | POSTERIOR MEDIASTINAL MASS | - | - | PRESENT | - | - |
| 95 | 1009083 | CA2+=8.7, ESR=82,AFP=0.92IU/ML | USG GUIDED | ANTERIOR MEDIASTINAL MASS | SCANTILY CELLULAR | SINGELY DISPERSED | PRESENT | - | - |
| 96 | 1023325 | - | USG GUIDED | POSTERIOR MEDIASTINAL LYMPH NODE | CELLULAR | LOOSELY COHESIVE CUSTERS AND SINGELY DISPERSED | PRESENT | - | - |
| 97 | 631597 | HIV=NR, CA2+=8.8 | CT GUIDED | ANTERIOR MEDIASTINAL MASS | - | - | - | PRESENT | PRESENT |
| 98 | 1027220 | | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | SINGELY SCATTERED | PRESENT | - | - |
| 99 | 104058 | - | EUS GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | DISPERSED | | | |
| 100 | 1087436 | - | EUS GUIDED | ANTERIOR MEDIASTINAL LYMPH NODE | - | - | - | - | - |
| 101 | 1112650 | B-HCG=22.72, AFP=11982,CEA=3.47,LDH=98 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | CELL CLUSTERS,TRBECULAE AND PAPILLAROID | PRESENT | - | - |
| 101 | 1103669 | CA2+=8.6 | USG GUIDED | ANTERIO MEDIASTINAL MASS | CELLULAR | CLUSTERS AND SINGELY DISSOCIATED | PRESENT | - | PRESENT |
| 102 | 1121064 | LDH=717,AFP=1.58,ESR=20, CA2+=8.2 | USG GUIDED | ANTERIOR MEDIASTINAL MASS | CELLULAR | SINGELY SCATTERED | PRESENT | - | - |

| SR. NO | MRD NO | INFLAMMATORY CELLS | SPECIAL STAINS | BIOPSY/CELL BLOCK | IHC | CYTOLOGICAL DIAGNOSIS |
|---|---|---|---|---|---|---|
| 1 | 857898 | LYMPHOID CELLS | ZN-POSITIVE | GRANULOMATOUS INFLAMMATION | - | GRANULOMATOUS LYMPHADENITIS-TB |
| 2 | 860894 | - | | SCANTILY CELLULAR | - | NEOPLASTIC POSSIBILY THYMOMA |
| 3 | 668121 | LYMPHOID CELLS | ZN-NEGATIVE | EXTENSIVE AREAS OF NECROSIS | - | MALIGNANT ASPIRATE- LYMPHOMA |
| 4 | 867362 | NEUTROPHILS | NOT DONE | - | - | GRANULOMATOUS LYMPHADENITIS- TB |
| 5 | 126906 | LYMPHOID CELLS | ZN-POSITIVE | MALIGNANT ROUND CELL TUMOR ?LYMPHOMA/LEUKEMIA | T-CELL LYMPHOBLASTIC LEUKEMIA/LYMPHOMA | MALIGNANT ASPIRATE- LYMPHOMA |
| 6 | 136808 | NEUTROPHILA & EOSINOPHILS | ZN-NEGATIVE | - | - | GRANULOMATOUS INFLAMMATION ?TB/SARCOIDOSIS |
| 7 | 96997 | LYMPHOID CELLS | ZN-NEGATIVE | - | - | MALIGNANT ASPIRATE WITH P/O CARCINOMA |
| 8 | 130202 | DEGENERATED NEUTROPHILS | ZN-NEGATIVE | - | - | GRANULOMATOUS INFLAMMATION?CAUSE |
| 9 | 69622 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 10 | 13593 | NEUTROPHILS,EOSINOPHILS, LYMPHOCYTES | ZN-NEGATIVE | FIBROCOLLAGENOUS TISUE WITH INFILTRATION BY PC/L/E | HODGKIN'S LYMPHOMA- CLASSICAL TYPE | MALIGNANT ASPIRATE-LYMPHOMA |
| 11 | 178785 | - | NOT DONE | - | - | MALIGNANT ASPIRATE-CARCINOMA |
| 12 | 148457 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 13 | 177997 | LYMPHOCYTES | NOT DONE | - | NEUROENDOCRINE CARCINOMA | MALIGNANT ASPIRATE |
| 14 | 175143 | LYMPHOCYTES AND PLASMA CELLS | NOT DONE | MALIGNANT GERM CELL TUMOR-SEMINOMA | PLAP & OCT3/4 STRONGLY POSITIVE | MALIGNANT ASPIRATE-SEMINOMA |
| 15 | 174261 | NEUTROPHILS AND LYMPHOCYTES | NOT DONE | - | - | NEOPLASM POSSIBLY THYMOMA |
| 16 | 195334 | - | ZN-NEGATIVE | - | - | GRANULOMATOUS LYMPHADENITIS-TB |
| 18 | 208711 | PIGMENTED FOAMY MACROPHAGES | NOT DONE | - | - | ANTHRO-SILICOSIS |
| 19 | 222314 | - | NOT DONE | | | NON DIAGNOSTIC |
| 20 | 228537 | - | NOT DONE | | | NON DIAGNOSTIC |
| 21 | 252088 | - | NOT DONE | - | - | MALIGNANT ASPIRATE POSSIBILITY OF MALIGNANT EPITHELIAL TUMOR |
| 22 | 239467 | LYMPHOCYTES | NOT DONE | | | CYSTIC LESION |
| 23 | 241494 | REACTIVE LYMPHOCYTES | ZN-NEGATIVE | - | - | GRANULOMATOUS LYMPHADENITIS-?TB/SARCOIDOSIS |
| 24 | 244749 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 25 | 244716 | REACTIVE LYMPHOID CELLS | ZN-NEGATIVE | - | - | GRANULOMATOUS LYMPHADENITIS |
| 26 | 355273 | PIGMENTED FOAMY MACROPHAGES | ZN-NOT DONE | SQUAMOUS CELL CARCINOMA | CK7, P63, CK5/6 = POSITIVE | MALIGNANT ASPIRATE-CARCINOMA |
| 27 | 441384 | FOAMY MACROPHAGES & MULTINUCLEATED GC | ZN-NON CONTRIBUTORY | - | - | NON-DIAGNOSTIC |
| 28 | 473300 | NEUTROPHILS | NOT DONE | METASTATIC CARCINOMATOUS DEPOSITS FROM GI ORIGIN | CK20,CDX2=POSITIVE; CK7,TTF-1=NEGATIVE | NON DIAGNOSTIC |
| 29 | 479177 | NEUTROPHILS | NOT DONE | NEUROENDOCRINE CARCIOMA GRADE 3 | CK, SYNAPTOPHYSIN, CHROMOGRANIN A= POSITIVE, MB-1=80% | MALIGNANT ROUND CELL TUMOR ?SMALL CELL CA ? MALIGNANT LYMPHOMA |
| 30 | 482870 | - | NOT DONE | EPITHELIAL MALIGNANCY FAVORS THYMIC CA | P63,CK5/6,CD117,P16,CD5,CK7= POSITIVE; CK20,TTF-1=NEG | EPITHELIAL NEOPLASM POSSIBLY MALIGNANT |
| 31 | 494406 | REACTIVE LYMPHOID CELLS | NON CONTRIBUTORY | - | - | GRANULOMATOUS LYMPHADENITS ?CAUSE |
| 32 | 493855 | REACTIVE LYMPHOID CELLS & FM | NOT DONE | - | - | REACTIVE HYPERPLASIA |

| SR. NO | MRD NO | INFLAMMATORY CELLS | SPECIAL STAINS | BIOPSY/CELL BLOCK | IHC | CYTOLOGICAL DIAGNOSIS |
|---|---|---|---|---|---|---|
| 33 | 42186 | REACTIVE LYMHOID CELLS & NEUTROPHILS | NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION ?CAUSE |
| 34 | 340870 | LYMPHOID CELLS | NOT DONE | | | NON DIAGNOSTIC |
| 35 | 533700 | NEUTROPHILS, LYMPHOCYTES,FM& GC | NOT DONE | | | NON DIAGNOSTIC |
| 36 | 392224 | EOSINOPHILS, LYMPHOCYTES, NEUTROPHILS | ZN & PAS-NEGATIVE | KIMURA;S DISEASE/ HODGKIN LYMPHOMA/ DRUG INDUCED | CD15 POSITIVE IN EOSINOPHILS, CD30 EQUIVOCAL | NON DIAGNOSTIC |
| 37 | 557954 | REACTIVE LYMPHOID CELLS | NOT DONE | - | - | METASTATIC CARCINOMATOUS DEPOSITS |
| 38 | 532384 | NEUTROPHILS, LYMPHOCYTES & LANGHANS GC | NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION |
| 39 | 571828 | DEGENERATED & VIABLE NEUTROPHILS | NOT DONE | | | MALIGNANT ASPIRATE- CARCINOMA |
| 40 | 562838 | - | NOT DONE | NEUROGENIC TUMOR WITH LOW PROLIFERATIVE INDEX | S100- POSITIVE MIB-1=1%, SMA,CD34= NEGATIVE | NON DIAGNOSTIC |
| 41 | 579053 | REACTIVE LYMPHOID CELLS | NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION |
| 42 | 580775 | FEW NEUTROPHILS | NOT DONE | - | - | NON DIAGNOSTIC |
| 43 | 588193 | - | NOT DONE | MALIGNANT ROUND CELL TUMOR POSSIBLY PNET | CK,EMA,CD99= POSITIVE, MIB-1=50% | HEMATOLYMPHOID MALIGNANCY |
| 44 | 599525 | NEUTROPHILS, LYMPHOCYTES, HISTIOCYTES | NOT DONE | - | - | MALIGNANT ASPIRATE- CARCINOMA |
| 45 | 628798 | REACTIVE LYMPHOID CELLS | NON-CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION |
| 46 | 277593 | REACTIVE LYMPHOID CELLS | NON- CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION |
| 47 | | REACTIVE LYMPHOID CELLS | ZN-NON CONTRIBUTORY | - | - | GRANULOMATOUSINFLAMMATION ?TB/SARCOIDOSIS |
| 48 | 178932 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 49 | 279863 | LYMPHOCYTES | NOT DONE | - | - | MALIGNANT ASPIRATE-SCC |
| 50 | 273169 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 51 | 294538 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 52 | 294538 | DEGENERATED NEUTROPHILS & LYMPHOCYTES | ZN-NEGATIVE | - | - | GRANULOMATOUS INFLAMMATION |
| 53 | 296888 | MATURE LYMPHOCYTES | NOT DONE | - | - | THYMIC NEOPLASM |
| 54 | 266710 | HISTIOCYTES | ZN-NEGATIVE | - | - | NON DIAGNOSTIC |
| 55 | 272031 | LYMPHOID CELLS | ZN-NEGATIVE | - | - | NON-DIAGNOSTIC |
| 56 | 312272 | - | NOT DONE | THYMOMA-AB TYPE | - | NON DIAGNOSTIC |
| 57 | 317877 | REACTIVE LYMPHOCYTES | NOT DONE | - | - | THYMOMA |
| 58 | 322582 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 59 | 340870 | REACTIVE LYMPHOID CELLS | ZN-POSITIVE | - | - | GRANULOMATOUS LYMPHADENITIS-TB |
| 60 | 344271 | DEGENERATED NEUTROPHILS | NOT DONE | CARCINOMA | - | MALIGNANT ASPIRATE-CARCINOMA |
| 61 | 382559 | REACTIVE LYMPHOID CELLS | ZN-NEGATIVE | - | - | NON DIAGNOSTIC |

| SR. NO | MRD NO | INFLAMMATORY CELLS | SPECIAL STAINS | BIOPSY/CELL BLOCK | IHC | CYTOLOGICAL DIAGNOSIS |
|---|---|---|---|---|---|---|
| 62 | 386950 | HISTIOCYTES &LYMPHOCYTES | ZN-NEGATIVE | INFLAMMATORY PATHOLOGY ACTE AND CHRONIC | - | INFLAMMATORY PATHOLOGY |
| 63 | 389728 | - | NOT DONE | NON-HODGKINS LYMPHOMA LARGE B-CELL TYPE | LCA,CD20,CD3=+, BCL2,BC6,CD10,MUM-1,CD30=NEG, MIB-1=70% | MALIGNANT ASPIRATE |
| 64 | 397810 | - | ZN-NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION-TB |
| 65 | 408552 | LYMPHOID CELLS | NOT DONE | NEOPLASM-THYMOMA | - | SPINDLE CELL NEOPLASM- THYMOMA/ NERVE SHEATH TUMOR |
| 66 | 411752 | FOAMY MACROPHAGES | NOT DONE | LARGE CELL NEUROENDOCRINE CARCINOMA | CK,LCA,CHROMOGRANIN A =+, SYNAPTOPHYSIN,TTF-1=NEG, MIB-1=90% | MALIGNANT ASPIRATE- LARGE CELL NHL/POORELY DIFFERENTITED CA |
| 67 | 686079 | - | NOT DONE | - | - | BENIGN CYSTIC LESION |
| 68 | 692209 | - | ZN-NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION |
| 69 | 624858 | LYMPHOID CELLS & LANGHANS GC | ZN-NON CONTRIBUTORY | | | GRANULOMATOUS INFLAMMATION-?TB/SARCOIDOSIS |
| 70 | 698031 | EXTRACELLULAR MUCIN | NOT DONE | | | NON DIAGNOSTIC |
| 71 | 701771 | - | NOT DONE | | | MALIGNANT ASPIRATE-CARCINOMA |
| 72 | 704541 | - | NOT DONE | | | NON DIAGNOSTIC |
| 73 | 704416 | REACTIVE LYMPHOID CELLS& LANGHANS GC | ZN-NON CONTRIBUTORY | | | GRANULOMATOUS LYMPHADENITIS-TB |
| 74 | 723020 | - | NOT DONE | HIGH GRADE NHL LIKELY PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA | LCA,MUM-1,BCL-6,CD23,CD20=POSITIVE, MIB-1=98% | MALIGNANT ASPIRATE-HEMATOLYMPHOID MALIGNANCY |
| 75 | 672472 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 76 | 37170 | SPINDLE CELLS | NOT DONE | - | - | NON DIAGNOSTIC |
| 77 | 672472 | NEUTROPHILS & LYMPHOCYTES | ZN-NEGATIVE | - | - | ACUTE SUPPURATIVE PATHOLOGY |
| 78 | 746433 | CASEOUS NECROSIS & LANGHANS, FOREIGN BODY GC | ZN-POSITIVE | - | - | GRANULOMATOUS INFLAMMATION-TB |
| 79 | 682824 | FEW LYMPHOCYTES | NOT DONE | - | - | NON DIAGNOSTIC |
| 80 | 751139 | REACTIVE LYMPHOCYTES & NEUTROPHILS | NOT DONE | - | - | NON DIAGNOSTIC |
| 81 | 761228 | REACTIVE LYMPHOCYTES & NEUTROPHILS | NOT DONE | MALIGNANT TUMOR POSSIBLY NEUROENDOCRINE | - | METASTATIC DEPOSITS FROM MALIGNANT ROUND CELL TUMOR-P/O SCC |
| 82 | 782757 | REACTIVE LYMOPHOID CELLS | NOT DONE | - | - | MALIGNANT ROUND CELL TUMOR POSSIBLY NHL |
| 83 | 796867 | REACTIVE LYMPHOID CELLS | ZN-NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION ?CAUSE |
| 84 | 813248 | REACTIVE LYMPHOID CELLS | ZN-EQUIVOCAL | - | - | REACTIVE HYPERPLASIA |
| 85 | 835928 | REACTIVE LYMPHOID CELLS & MULTINUCLEATED GC | ZN-NON CONTRIBUTORY | - | - | GRANULOMATOUS INFLAMMATION-SARCOIDOSIS |
| 86 | 888131 | SHEETS OF NEUTROPHILS | NOT DONE | MALIGNANT NEOPLASM-CARCINOMA | - | MALIGNANT ASPIRATE |
| 87 | 899094 | - | NOT DONE | - | - | NON-DIAGNOSTIC |
| 88 | 191371 | REACTIVE LYMPHOID CELLS | ZN-NEGATIVE | GRANULOMATOUS INFLAMMATION- SARCOIDOSIS | - | GRANULOMATOUS INFLAMMATION ?TB/SARCOIDOSIS |
| 89 | 912347 | NEUTROPHILS | ZN,PAS,GMS-NEGATIVE | - | - | ATYPIA-RADIATION INDUCED CHANGES |
| 90 | 945549 | NEUTROPHILA & LYMPHOCYTES | NOT DONE | SQUAMOUS CELL CARCINOM LIKELY PRIMARY THYMIC CARCINOMA | CK,CD117,P40,CD5=+ , TTF-1,SYNAPTOPHYSIN,CHROMOGRANIN A = NEG | MALIGNANT ASPIRATE-METASTATIC CARCINOMATOUS DEPOSITS |
| 91 | 963973 | - | NOT DONE | - | - | NON DIAGNOSTIC |
| 92 | 964071 | LYMPHOID CELLS | NOT DONE | - | - | GRANULOMATOUS LYMPHADENITIS ?CAUSE |
| 93 | 1006973 | LYMPHOCYTES | NOT DONE | MALIGNANT ROUND CELL TUMOR | - | MALIGNANT ROUND CELL TUMOR |

| SR. NO | MRD NO | INFLAMMATORY CELLS | SPECIAL STAINS | BIOPSY/CELL BLOCK | IHC | CYTOLOGICAL DIAGNOSIS |
|---|---|---|---|---|---|---|
| 94 | 992720 | FOAMY MACROPHAGES | NOT DONE | SCWANIAN RICH NEUROBLASTIC TUMOR | SYNAPTOPHYSIN,NSE=+ IN GANGLION CELLS & SCWANIAN STROMA MIB-1=05% S100 IS + IN SCWANIAN STROMA | NEOPLASM |
| 95 | 1009083 | FEW NEUTROPHILS AND HISTIOCYTES | NOT DONE | - | - | LYMPHOMA |
| 96 | 1023325 | LYMPHOCYTES, FOAMY MACROPHAGES | NOT DONE | SMALL CELL CARCINOMA | NOT DONE | CARCINOMA POSSIBLY NEUROENDOCRINE |
| 97 | 631597 | LYMPHOCYTES,NEUTROPHILS & MACROPHAGES | ZN-POSTIVE | TUBERCULOSIS WITH CANDIDIASIS | NOT DONE | GRANULOMATOUS INFLAMMATION-TUBERCULOSIS |
| 98 | 1027220 | NEUTROPHILS, LYMPHOCYTES | NOT DONE | - | - | MALIGNANT ASPIRATE-ROUND CELL TUMOR POSSIBLY SMALL CELL NEC |
| 99 | 104058 | | NOT DONE | - | - | MALIGNANT ASPIRATE-HEMATOLYMPHOID MALIGNANCY |
| 100 | 1087436 | LYMPHOID CELLS | ZN=POSITIVE | - | - | GRANULOMATOUS LYMPHADENITIS -TB |
| 101 | 1112650 | NEUTROPHILS & LYMPHOCYTES | NOT DONE | GERM CELL TUMOR-IMMATURE TERATOMA | | MALIGNANT ASPIRATE-NON SEMINOMATOUS GERM CELL TUMOR |
| 101 | 1103669 | - | NOT DONE | NEUROENDOCRINE CARCINOMA SMALL CELL TYPE PRIMARY FROM LUNG | TTF-1, SYNAPTOPHYSIN CHROMOGRANIN, CK= POSITIVE & MIB-1=95% | MALIGNANT ROUND CELL TUMOR |
| 102 | 1121064 | NEUTROPHILS AND EOSINOPHILS AND FM | NOT DONE | PRECURSOR T-LYMPHOBLASTIC LYMPHOMA | TdT,CD3,CD8,CD1a,CD5=POSITIVE & CD34,CD20,CD117, MPO=NEG | MALIGNANT ASPIRATE-LYMPHOMATOUS PROCESS |

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Date 22/4/2021

The Principal,
DMC, Ludhiana

**Subject:** Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Rashi Aggarwal**, a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

**Topic Plan of Thesis**
Cytopathological spectrum of mediastinal lesions

Supervisor
Dr. Pavneet Kaur Selhi
Prof.,
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Co-Supervisor
Dr. Ruchita Tyagi
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Assoc. Prof.,
Dept. of Radio-diagnosis,

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,( if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

*Note :*

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

# CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2019

DR. RASHI AGGARWAL

DEPARTMENT OF PATHOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

# ABSTRACT OF PLAN OF THESIS

| | |
|---|---|
| Title | CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS |
| For the degree of | MD (PATHOLOGY) |
| Name of the candidate | Dr. Rashi Aggarwal |
| Supervisor | Dr Pavneet Kaur Selhi, Professor, Department of Pathology, DMCH, Ludhiana |
| Co-supervisor(s) | Dr. Ruchita Tyagi, Assistant Professor, Department of Pathology, DMCH, Ludhiana<br>Dr. Siddharth Prakash, Associate Professor, Department of Radiodiagnosis, DMCH, Ludhiana |
| Institution | Dayanand Medical College and Hospital, Ludhiana |
| University | Baba Farid University of Health Sciences, Faridkot |

**Introduction**: Mediastinal lesions are uncommon in routine clinical practice. They can be broadly classified into non neoplastic and neoplastic lesions. FNAC has been increasingly utilised as a minimally invasive procedure for the diagnosis of mediastinal lesions.

**Aims & Objectives**: To study the cytomorphological features of all mediastinal lesions and to correlate them with the clinico-radiological profile, histopathological findings and IHC wherever possible.

**Material & Methods**: This study will be conducted in Dayanand Medical College And Hospital, Ludhiana for a period of 5 years from 1st july 2016 to 30th june 2021 (one and half years prospective and three and a half years retrospective) .The smears received in the cytology lab from guided FNAC of mediastinal lesions will be analysed and cell blocks will be made whenever possible. Special stains will be done wherever necessary.

**Clinical Significance**: FNAC for mediastinal lesions has become an established diagnostic procedure with excellent results worldwide. The main aim is to categorise the lesion as neoplastic or non neoplastic and further as benign or malignant. This will enable the clinicians to manage and treat the cases effectively .In this study we also plan to correlate the cytomorphological features with the clinico-radiological findings, histopathological findings and IHC wherever possible.

**Keywords**: Mediastinal Lesions, FNAC, Clinico-Radiological and Histopathological findings

| (Signature) | (Signature) | (Signature) | (Signature) | (Signature) |
|---|---|---|---|---|
| Candidate | Co-supervisor | Co-supervisor | Supervisor | Principal |

## CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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**Co-Supervisor(s)**

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Place : _____

Date : _____

# APPROVAL PROFORMA
# BY RESEARCH & ETHICAL COMMITTEE
# DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

| | |
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| **Name of candidate** | Dr. Rashi Aggarwal |
| **Department** | Pathology |
| **Topic of Thesis** | CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS |
| **Likely date of appearing in PG examination** | May 2022 |
| **Date of enrollment** | 6TH May,2019 |
| **Name of Head of Department** | Dr. Neena Sood |
| 1) **Supervisor**<br>2) **Co-Supervisor(s)** | Dr. Pavneet Kaur Selhi<br>Dr. Ruchita Tyagi<br>Dr. Siddharth Prakash |
| **Signature of Members of Research Committee with Stamp** | **Signature of Members of Ethics Committee with Stamp** |
| Dr. Jaspal Singh<br>(Professor & Head, Surgery) | Mr. A K Jindal<br>(Member, Ethics Committee) |
| Dr. Dinesh Gupta<br>(Professor & Head, Medicine) | Dr. Anu Sharma<br>(Professor, Anatomy) |
| Dr. Sandeep Kaushal<br>(Assistant Dean Academics) | Dr. Deepinder K Chhina<br>(Professor & Head, Microbiology) |
| Dr. Rajoo Singh Chhina<br>(Dean Academics) | Dr. Neena Sood<br>(Professor & Head, Pathology) |
| Dr. Gurpreet S Wander<br>(Vice Principal) | Dr. Gurpreet S Wander<br>(Vice Principal) |
| | Dr. Gagandeep Singh<br>(Secretary, Ethics Committee)<br>Professor & Head, Neurology) |

**Approved: Yes / ~~No~~**

**Dr. Sandeep Puri**
**Chairperson**
**Research Committee**

Chairperson
Research Committee

**Approved: Yes / ~~No~~**

**Prof. Arvind Malhotra**
**Chairperson**
**Ethics Committee**

Chairperson
Ethics Committee

# BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

## PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

| | | |
|---|---|---|
| 1 | NAME OF THE CANDIDATE AND ADDRESS | Dr. Rashi Aggarwal<br>10 New laxmi pura adjoining deva mandir, Jalandhar<br>Punjab<br>Pin-144001 |
| 2 | NAME OF THE INSTITUTE | Dayanand Medical College and Hospital, Ludhiana |
| 3 | COURSE OF STUDY AND SUBJECT | MD Pathology |
| 4 | DATE OF ADMISSION OF COURSE | 06-05-2019 |
| 5 | TITLE OF THE TOPIC | CYTOPATHOLOGICAL SPECTRUM OF MEDIASTINAL LESIONS |

## 6. BRIEF RESUME OF THE INTENDED WORK

### 6.1 NEED FOR THE STUDY

Mediastinal tumors are rare comprising only 3% of tumors occurring within the chest.[1] Amongst these, nearly 66% are malignant. Pre-operative diagnosis of mediastinal masses is a challenging task owing to the non-specific clinico-radiological signs and technical difficulty in performing FNAC. The investigation of choice for the detection of mediastinal masses is CT scan.MRI is of help in further categorization of the lesions. CT-guided FNAC is a safe, useful and cost effective method for the diagnosis of mediastinal masses. However, close proximity to the vital organs can be a hindrance for this technique. Though Surgical pathology is often considered to be the gold standard for diagnosis, FNAC of mediastinal masses allows for rapid on-site evaluation and triaging of material for ancillary studies. It has garnered widespread acceptance among clinicians and their patients. Because of the minimally invasive nature of this technique, it is well tolerated by patients without any major complications. It is also a cost effective diagnostic tool with a high sensitivity and specificity of almost 78% to 98%, respectively. It provides useful information such as differentiating a neoplastic lesion from a non neoplastic one and further recognizing the lesion as benign or malignant.

Fine needle aspiration cytology (FNAC) is a relatively non-invasive technique that can be used alone or in conjunction with core needle biopsy (CNB) prior to therapy, allows for rapid on-site evaluation and is helpful in triaging material for ancillary studies such as flow cytometry, immunohistochemistry and molecular studies. When many etiologic cells of origin is not diagnosed accurately by cytology alone, then the CNB for small histology section is recommended as an initial investigation method with FNAC. However repeated FNAC procedure due to inadequate cytological material delays the diagnosis and specific therapy, which increases the risk of invasive surgical procedures and the tissue sample obtained by CNB allows more architectural, cytological and immunohistochemical studies, which increases diagnostic accuracy and sensitivity of CNB over FNAC. But

FNAC is used as a initial procedure when the probability of carcinoma is high. FNAC and/or core biopsy under ultrasound or CT scan allows adequate tissue sampling with the least risk to the patients. The procedure is largely safe, easy to perform and well tolerated with reduced medical care cost as it eliminates the need for more extensive diagnostic surgical procedures and hospital stay. Clinical background and radiological correlation further support the cytopathologist to make a firm diagnosis.

Thus the conventional transthoracic FNA and/ or biopsy for mediastinal lesions still hold its role due to easy procedure, low cost, easy to train and learn in low infrastructure units.

Ultrasonographic or CT-guided FNAC is not only a simple technique due to its very low complication rate and high diagnostic accuracy , but it also should be considered as the initial method of choice in mediastinal lesions.

A major advantage of FNAC is that immediate cytological examination of the specimen is possible and then pathologist can direct the clinician appropriately.

In conclusion, FNAC is a relatively non-invasive technique that can yield a rich amount of information through smears , thin layer liquid-based preparations, cytospins and other preparations and as well as through ancillary techniques such as immunohistochemistry , flow cytometry and molecular assays. Thus mediastinal FNAC is both fairly sensitive and very specific and is a valuable technique in the diagnosis of mediastinal masses.

## 6.2 REVIEW OF LITERATURE

The mediastinum is the central portion of the thoracic cavity, limited by pleural cavities laterally, thoracic inlet superiorly and the diaphragm inferiorly. It is further divided into superior, anterior, middle and posterior compartments.[2]

The mediastinum is a site having many vital anatomic structures, due to which imaging techniques are often required to guide the biopsy needle to sample the target area.[3] FNAC is commonly used to sample tumors in all mediastinal compartments. Although clinical history, physical examination, radiological findings and location of masses in the mediastinum often help in making the diagnosis, but tissue diagnosis is the gold standard for the final diagnosis and plan management of mediastinal lesions.[4]

Majority of tumors are seen in the anterior mediastinum.[5-7] Nearly 50% of all the mediastinal masses are anterior mediastinal tumors which include thymoma, teratoma, thyroid lesions and lymphoma.[3] Among lymphomas 50-70% of primary mediastinal lymphomas are hodgkin type and diffuse large B-cell lymphoma and acute lymphoblastic lymphoma are the common non-hodgkin lymphomas found in the mediastinum.[8] In the middle mediastinum, the lesions found are typically congenital cysts whereas neurogenic tumors commonly arise in the posterior mediastinum[4] are neurilemmomas, neurofibromas and ganglioneuromas.[9]

## CYTOLOGY OF MEDIASTINUM MASSES

Aspirates from the mediastinum is divided into neoplastic and non neoplastic lesions which is further divided into benign and malignant categories.[10] Neoplastic lesions consists of metastatic adenopathy of the mediastinal nodes, small cell lung cancer, neuroendocrine carcinoma, Non Hodgkin's, Hodgkin's lymphoma, thymoma thymolipoma, germ cell tumor , and carcinoid tumor . Among the non-neoplastic lesions tuberculosis is the most common.

Cytology of Non Hodgkin's lymphoma shows dispersed monotonous population of cells with coarse granular chromatin and lymphoid globules in background.

Hodgkin lymphoma shows Reed–Sternberg cells, Hodgkin cells in the background of lymphocytes, plasma cells, eosinophils, and histiocytes.

Cytology of thymic neoplasm reveals cohesive tissue fragments of oval to spindle epithelial cells admixed with lymphoid cells.

Carcinoid tumor is suggested by dispersed monotonous small neoplastic cells with rounded to oval nuclei with salt-pepper chromatin, inconspicous nucleoli with moderate amount of reddish granular cytoplasm.

Features of teratoma are keratinous debris, squamous epithelial cells, glandular epithelium with hair shaft material.

Germinoma shows dispersed as well as loose clusters of large cells having rounded nuclei, prominent single or multiple nucleoli and abundant fragile cytoplasm against a tigroid background containing lymphocytes.

Cytological evaluation allows for lesion to be categorized as neoplastic and further into benign and malignant. However, making a specific diagnosis is not always possible by FNAC . In such cases specimens by Core needle biopsy (CNB) are usually required for more precise diagnosis, allowing histopathological and immunohistochemical studies.[11-13]

It is possible to establish histological subtypes on CNB.[14]

**1. Non Diagnostic**

This includes cases with:

-Insufficient quantitative and/or qualitative cellular material to make a cytological diagnosis.

-Aspirates with benign elements only, in a setting of clinically or radiologically defined mass.

**2. Non Neoplastic**

This includes specimen lacking evidence of neoplastic process.

Inflammatory, metaplastic, infective and reactive lesions which includes acute, chronic and granulomatous like tuberculosis, sarcoidosis, Cysts like thymic cyst, bronchogenic cyst.

**3. Neoplasm**

It is further divided into 2 categories-

a.) Benign neoplasm- thymoma, lipoma, thymolipoma , neurogenic tumors etc.

b.) Malignant – aspirates which are diagnostic of malignancy such as Hodgkin's, Non-Hodgkin's lymphoma, germ cell tumors, carcinoid tumor, neuroendocrine carcinoma, sarcomas and metastasis.

**4. Suspicious For Malignancy**

This category includes aspirates which are highly suggestive of malignancy but not definitive.

FNAC of mediastinal masses allows for rapid on-site evaluation and triaging of material for ancillary studies. A study by Ramakant Dixit et al[15] included144 patients who had undergone ultrasound-guided FNAC and/or core biopsy for mediastinal lesions. Out of 139 cases, 93 cases were neoplastic in nature (67%), 32 were nonneoplastic (23%), and 14 remained inconclusive (10%). Among neoplastic mediastinal lesions, metastatic carcinoma (37.4%) was the most common neoplastic lesion, followed by Non-Hodgkin's lymphoma (12.2%), Hodgkin's lymphoma (7.1%), thymic lesions (3.5%), etc. Among nonneoplastic conditions, tuberculosis was the most common lesion (20.1%). An accurate tissue diagnosis was made in 89.9% cases by FNAC or core biopsy of mediastinal lesions in this study.

Alan Marcus et al[16] found that the overall sensitivity for mediastinal mass FNAC was 78% and the overall specificity was 98% in their study of 77 mediastinal FNAC.

Another retrospective study by Senjuti Dasgupta[1] et al of 22 cases studied CT guided FNACs performed in 15 patients. These included 4 cases of thymic lesions, 3 of extragonadal GCT, 5 of lymphoma, 2 of schwannoma, and one case of ganglioneuroma. On histopathological examination, 2 cases of thymic lesions were diagnosed as thymic hyperplasia and the rest as thymoma.

A Study by Preeti Sharma et al[17] reviewed 60 cases in which, 22 were anterior, 20 were middle and 18 were posterior mediastinal masses. The most common diagnosis was thymoma (12 cases) followed by lymphoma, tubercular lymphadenopathy and schwannoma, neurofibroma, extragonadal germ cell tumours, thymic cyst,

bronchogenic cyst, retrosternal goitre, ganglioneuroma and neuroblastoma, and lipoma and thymolipoma. FNAC was done in 54 cases of which 7 cases yielded inadequate material.

A study conducted by Jitendra G et al[19] on 50 patients who underwent CNB and FNAC for their anterior mediastinal masses , 35 (71.42%) patients were diagnosed correctly by FNAC and cyto-histologic correlation was found; whereas 14 (28.57%) patients were not diagnosed definitely by FNAC. Overall sensitivity was 71.42% for FNAC.

Parimal et al[18] reported a series of 5 cases of Lennert's lymphoma which is a variant of peripheral T-cell lymphomas. They concluded that classical Hodgkin's lymphoma is a close mimicker of Lennert's lymphoma and suggested T cell gene rearrangement studies when distinction cannot be made on morphology and IHC.

## 6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the detailed cytomorphological features of all mediastinal lesions.
2. To correlate them with clinico-radiological profile and histopathology with IHC wherever possible.

## 7. MATERIALS AND METHODS

### 7.1 Source of Data

Fine needle aspiration smears from mediastinal lesions received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of one and half years prospective and three and a half years retrospectively (1st July 2016 - 30th June 2021) will be analysed.

### 7.2 METHOD OF COLLECTION OF DATA

**INCLUSION CRITERIA**

FNAC samples from mediastinal lesions received in the Cytology Lab of the pathology department which will include.

1. FNAC slides received in the department after guided aspiration (ultrasonography and/or CT guidance and/or endoscopic ultrasonography).
2. Prepared and stained slides for review from an outside centre.

**EXCLUSION CRITERIA-**

Samples obtained from lesions other than from mediastinum.

**PROCEDURE**

After informed consent, radiologically and EUS guided fine needle aspiration (FNAC) will be done using 23 guage needle attached to 20cc disposable plastic syringe by taking aseptic precautions .Under the radiological guidance ,aspiration will be performed and slides will be prepared immediately. One of the slides will be utilized for rapid on site evaluation for adequacy by staining with Toulidine Blue stain. Two slides will be wet fixed in 95% ethanol for Papanicolaou stain and Hematoxylin and Eosin stains. The remaining smears will be air dried and stained by May Grunwald Giemsa stain. FNA samples collected in separate pass will be fixed in 10% formalin, processed and embedded to make cell blocks. Sections will be stained by H & E stain. Special stains will be done wherever necessary.

**DURATION OF STUDY**

Prospective: One and a half years (1st Jan 2020- 30th June 2021)

Retrospective: Three and a half years (1st July 2016 –31st Dec. 2019 )

**Study Design**

This is a prospective and retrospective study.

**OUTCOME**

The smears obtained by FNA (ultrasound/CT/EUS guided) of all mediastinal lesions will be analysed in this study. The cytological findings will be correlated with the clinico-radiological profile, cell block findings, histopathological findings, special stains and IHC findings wherever possible.

**STATISTICAL ANALYSIS**

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

**7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.**

Yes

**7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?**

Yes

## 8. LIST OF REFERENCES


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## PROFORMA

Serial no.- Asp. No Date-

Name Age Sex

MRD No. Phone No.

Address

Clinical features with duration

-Fever -Cough

-Shortness of breath -Chest pain

-Hemoptysis -Loss of weight and appetite

Co -morbities-

-COPD -DM -HTN

Past History-

-Previous history of TB -Any history of empirical ATT

-H/O Immunosupression-

Clinical Examination:

Radiological Findings-

Investigations-

CBC with PBF ESR

S.Calcium LDH

Serum Tumor Marker S. ACE levels
HIV Serology

**Signature of Candidate** **Signature of Supervisor**

FNAC Findings:

-Cellularity –

-Architectural Pattern-

-N:C ratio

-Nuclei

-Nucleoli

-Cytoplasm

-Necrosis

-Granuloma

-Inflammatory cells-Acute

-Chronic

- Foamy Macrophages

-Giant Cells

-Fungal spores/Hyphae

-Special Stains- AFB-1%/ 20% -PAS -GMS

Cytopathological Diagnosis:

Histopathology- Cell Block/ Surgical pathology speciemen

Findings-

Histopathological Diagnosis-

IHC (If any)

Final Diagnosis

**Signature of Candidate** **Signature of Supervisor**